

Interim Session, Rochester, Minnesota, November 29-30, 1958  
Semi-Annual Meeting, Board of Regents, Minneapolis, Minnesota,  
December 1, 1958

VOLUME XXXIV

NUMBER 5

# **DISEASES**

*of the*

# **CHEST**

OFFICIAL PUBLICATION



PUBLISHED MONTHLY

NOVEMBER  
1958

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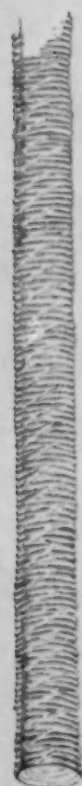
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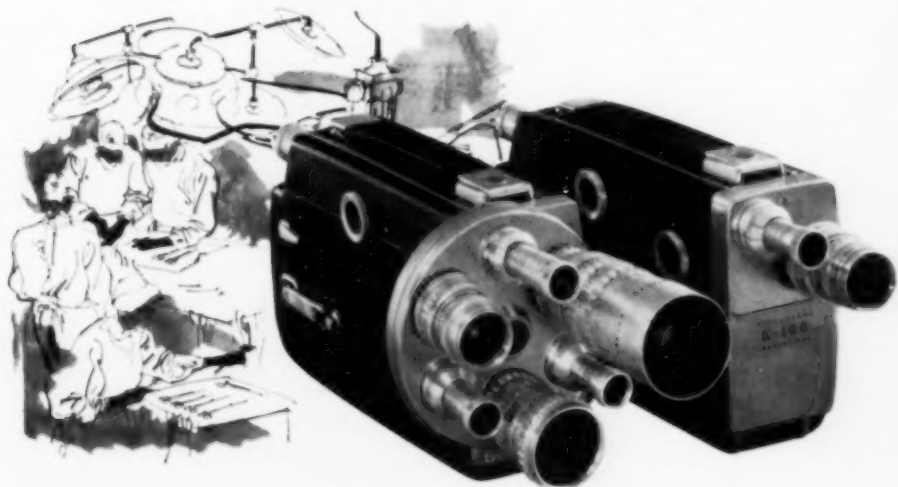
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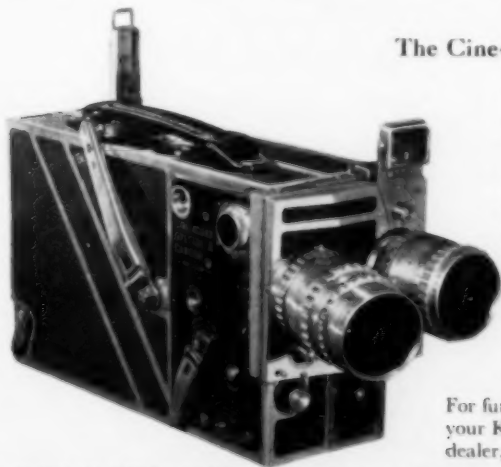


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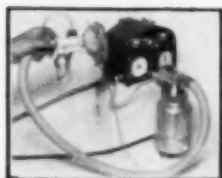
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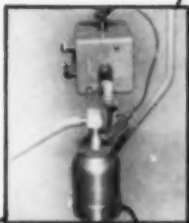
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*Considerations in Humidification by Nebulization: Ivan Cushing, MD, and William F. Miller, MD. Diseases of the Chest, Oct. 1958, Vol. XXXIV, No. 4.*

*An Aerosol Method of Producing Bronchial Secretions in Human Subjects: A Clinical Technique for the Detection of Lung Cancer. Hylan Bickerman, MD, FCCP; Edith Sproul, MD, and Alvan L. Barach, MD, FCCP. Diseases of the Chest, April, 1958, Vol. XXXIII, No. 4.*



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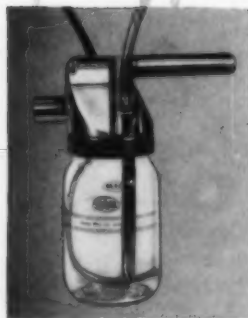


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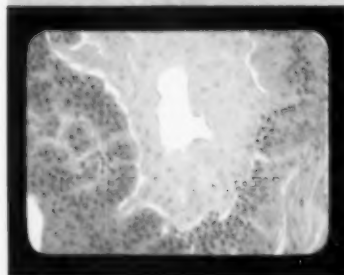
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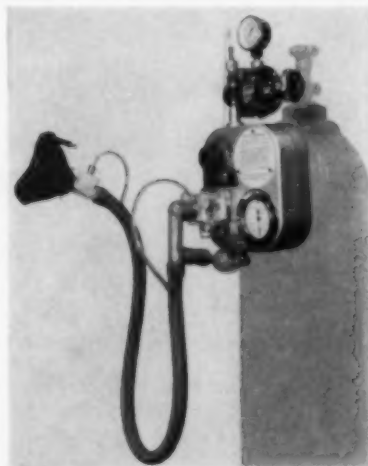
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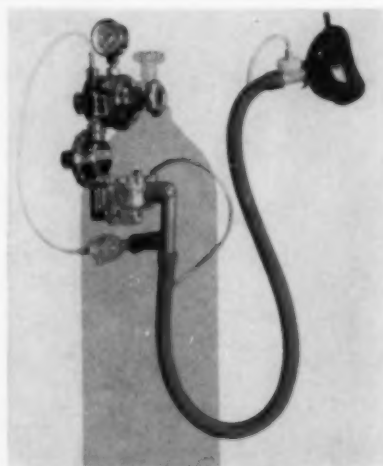
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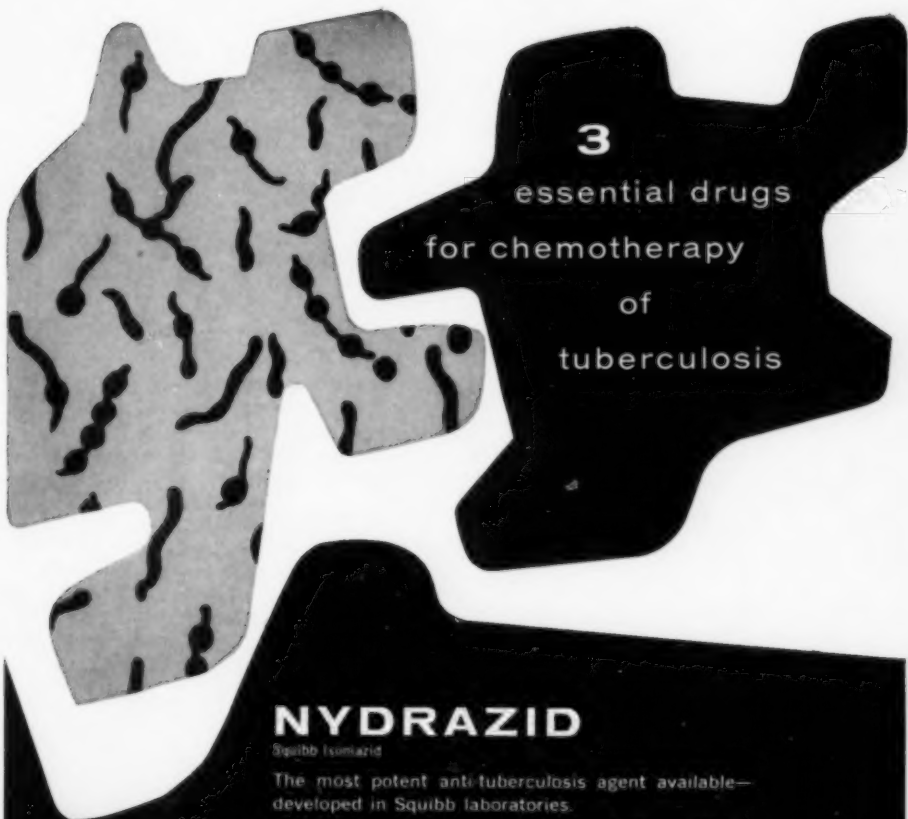
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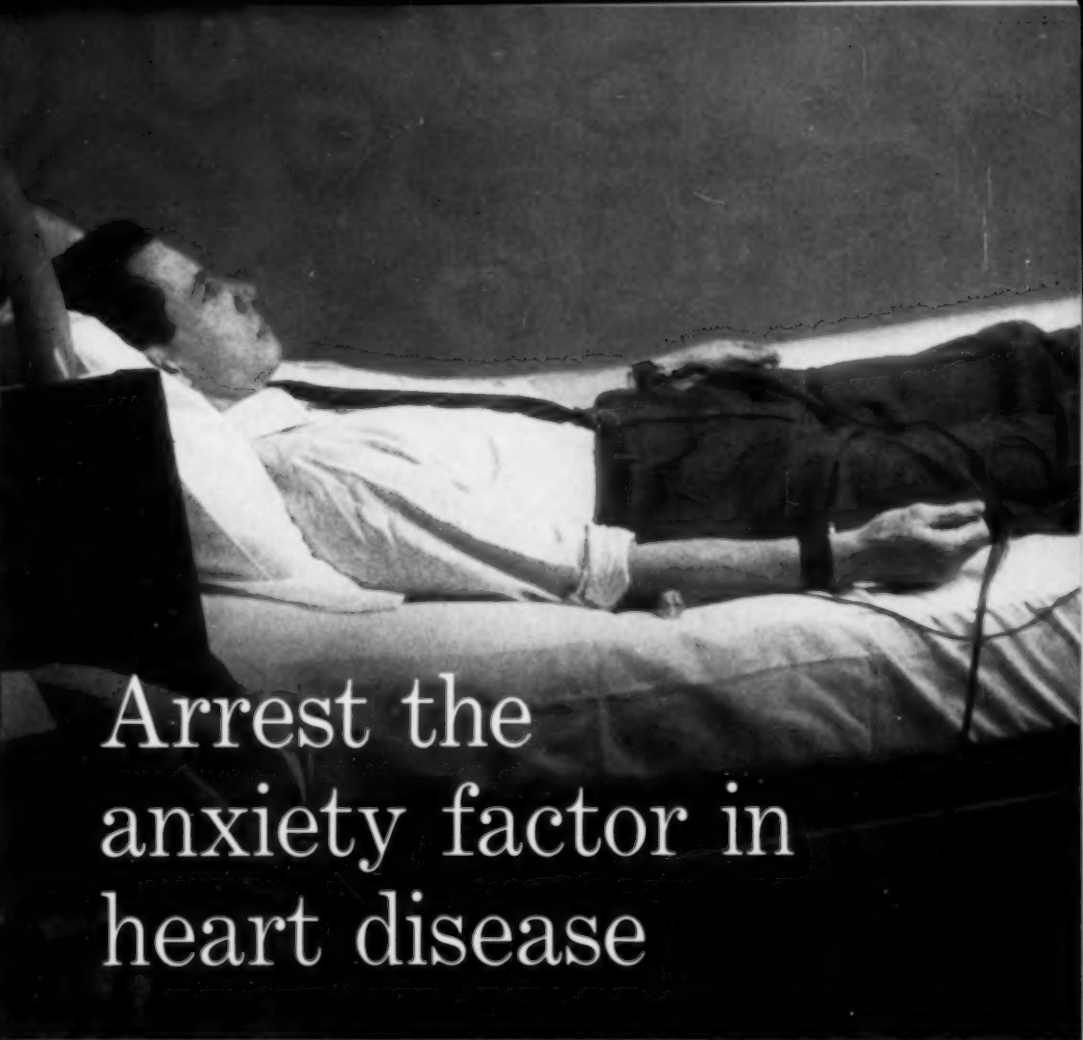
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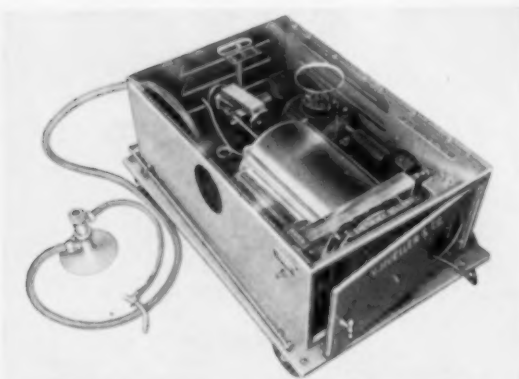
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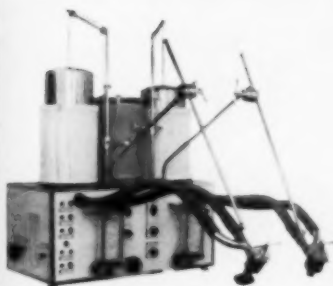
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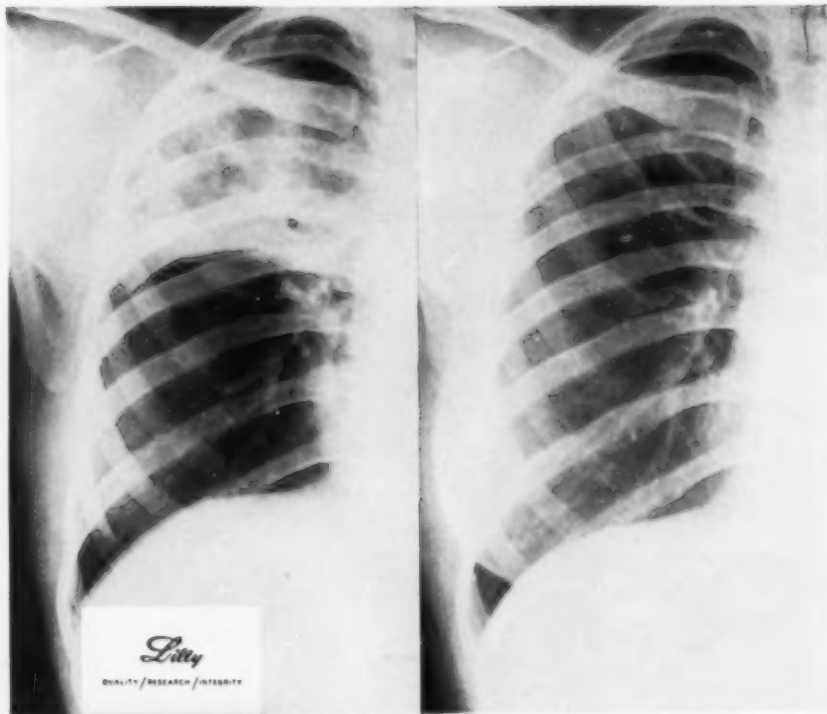
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# DISEASES of the CHEST

VOLUME XXXIV

NOVEMBER, 1958

NUMBER 5

## Sensitivity to Tuberculin, Histoplasmin and Coccidioidin Among High School Students in Northwestern Georgia\*

PHYLLIS Q. EDWARDS, M.D., CECIL F. JACOBS, M.D.

Washington, D. C.

and DOROTHY BARFIELD, R.N.

Dalton, Georgia

Skin testing surveys of school-age groups with tuberculin and, in some localities, also with histoplasmin and coccidioidin, are gaining recognition as a useful public health procedure. The rapidly changing tuberculosis picture in most communities, together with the apparent need to reduce radiation exposure to a minimum, means that the tuberculin test is emerging as an important method for measuring the progress of tuberculosis control programs. Testing, in addition, with fungus antigens is becoming more or less mandatory in areas where fungus infections complicate the picture.

The present report adds to the growing body of experience collected during the last few years on the value to a community of results obtained from a carefully conducted skin-testing survey of school-age populations.<sup>1-9</sup> The immediate stimulus to undertake the survey arose during the course of reviewing the tuberculosis case register at the Dalton-Whitfield and Murray County Health Department. Some of the patients on the register had had repeatedly negative sputum examinations for tubercle bacilli and some, in addition, did not react to tuberculin. The high frequency of pulmonary calcifications on routine x-ray films, which could not be attributed to tuberculosis, created a great deal of speculation as to the etiological factor. Histoplasmosis came to mind as a diagnostic possibility, as the Whitfield-Murray area is situated in the northwestern corner of Georgia on the fringe of the histoplasmosis endemic area; yet the prevalence of infection with the fungus in the immediate vicinity of Whitfield County was not known. The time had come to find out.

### *Study Population and Procedures*

The skin-testing survey, supplemented with 70 mm. x-ray films, was carried out in March, 1957. It was organized by the Dalton-Whitfield

\*From the Tuberculosis Program, Division of Special Health Services, Public Health Service, U. S. Department of Health, Education and Welfare; and the Dalton-Whitfield and Murray Counties Health Department, Dalton, Georgia.

County and Murray County Health Departments. A note signed by the District Director of Public Health was sent to the parents of all high school students informing them that during a specified two-week period a survey would be conducted for the purpose of finding out how many students had had tuberculosis or fungus infection, and that a representative of the Health Department would be at each school during the survey to answer questions the students or parents might have about the program. A brief statement accompanying the note, and newspaper articles, described the general characteristics of histoplasmosis and coccidioidmycosis and why the Health authorities need to distinguish between these two fungus infections and tuberculosis. Mr. Clifford Hale, Superintendent of Dalton schools, Mr. Albert Davis, Superintendent of Whitfield County Schools, Mr. Ray Bagley, Superintendent of Murray County Schools, and all school principals gave their enthusiastic support which assured the success of the project.

The survey included the six public high schools in the two counties (fig. 1). Two of the schools are located in Dalton: Dalton High, for white students living in the city, and Emory High for all Negro students in both Whitfield and Murray Counties. White students living in the rural parts of the area attend one of the four rural high schools, whichever is nearest their home. The total enrollment for the six schools, as shown in table 1, was estimated to be just over 2,400, and 2,112 (87.3 per cent) of the students were tested and x-rayed. Participation was highest, almost 95 per cent, in Valley Point High School and just over 80 per cent in both Murray and Emory High Schools.

The testing and reading was done by a field research team from the Tuberculosis Program of the Public Health Service. Each student was tested simultaneously with histoplasmin, coccidioidin and tuberculin. Two

TABLE I  
NUMBER OF STUDENTS ENROLLED, AND NUMBER AND PER CENT  
WITH COMPLETED TESTS, FOR THE SIX HIGH SCHOOLS  
IN WHITFIELD-MURRAY COUNTIES, GEORGIA

High School	Number		Per Cent Completed Tests
	Enrolled	Completed Tests	
Murray	491	402	81.9
North Whitfield	537	486	90.5
Valley Point	396	375	94.7
Westside	222	192	86.5
Dalton	651	559	85.9
Total white	2297	2014	87.7
Emory (Negro)	121	98	81.0
Total all students	2418	2112*	87.3

\*Includes one student not tested with histoplasmin.

tests were given in one forearm, and one in the other, by intracutaneous injection of 0.1 ml. The products used for the survey were histoplasmin H-42 prepared by Dr. Arden Howell, Jr. of the Public Health Service; coccidioidin C-24, prepared by Dr. Charles E. Smith of the University of California; and tuberculin PPD-S, the international standard PPD, prepared by Dr. Florence Seibert of the Henry Phipps Institute. For study purposes, the histoplasmin was used in two dilutions, the standard 1:100 dilution and a 1:50 dilution, given alternately as the students came to be tested. Coccidioidin 1:100 dilution and the 5 TU (0.0001 mg.) dose of PPD-S were given to all students. All products were labelled in code on the bottles and the members of the testing team were not told what the bottles contained.

Reactions were read in 48 (or 72) hours by measuring and recording the transverse diameter of palpable induration. All readings (except in Emory High) were done by one experienced nurse.

Photofluorograms of the chest were taken at the time of the skin testing by a mobile unit provided by the Georgia Department of Public Health, through the courtesy of Dr. Clara Barrett. The films were read independently by two Public Health Service physicians who had no knowledge of the skin test results and who simply interpreted the films as normal or as showing evidence of calcification (definite or possible), infiltration, other (non-tuberculous) pathology or a combination of findings.

History of all places of residence since birth was also obtained for each student by direct questioning at the time of the testing.

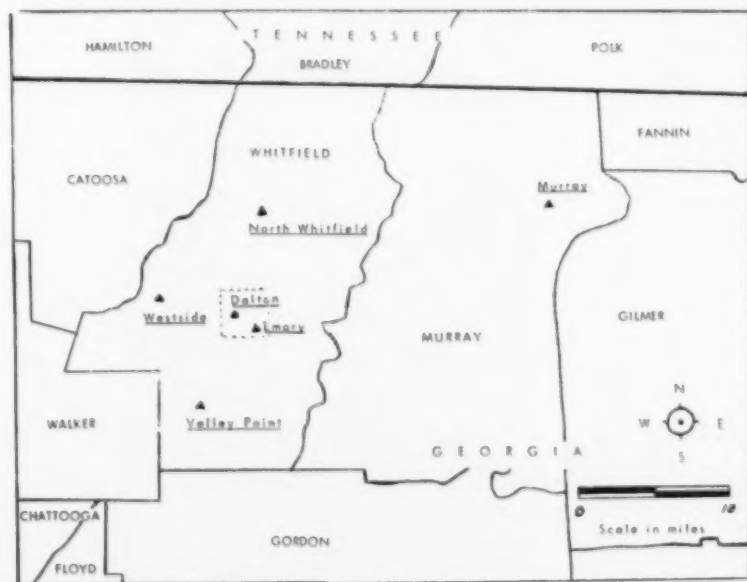


FIGURE 1: Map of Whitfield and Murray Counties, Georgia, showing location of the six public high schools and the adjoining counties.



*Results**Tuberculin sensitivity*

The frequency distribution by size of reactions to the 5 TU dose of PPD is given in figure 2, where the horizontal axis shows the diameter of induration (in 2 mm. groups) and the vertical axis shows the percentage of reactions of each specified size. More than 75 per cent of the tuberculin reactions were recorded as 0 or 1 mm., about 12 per cent as 2 or 3 mm. and about 3 per cent as 4 or 5 mm. For reactions of 6 to 25 mm., the frequencies were very low and nearly the same for each 2 mm. grouping but with a slight indication of a peak at 14-17 mm. There is no clear-cut separation of the distribution into two groups. The very large reactions, which can be presumed to represent tuberculous infection, merge with the very small reactions, which are undoubtedly negative.

Interpretation of the tuberculin reactions in the present study may, however, be based on material from other reports.<sup>10-12</sup> Many of the reactions measuring less than 10 mm. to the 5 TU test, and this is particularly true in the southeastern part of the country, apparently represent non-specific (heterologous) sensitivity. Reactions in the range from about 3 or 4 to perhaps 9 mm. represent a mixture of positive, negative and

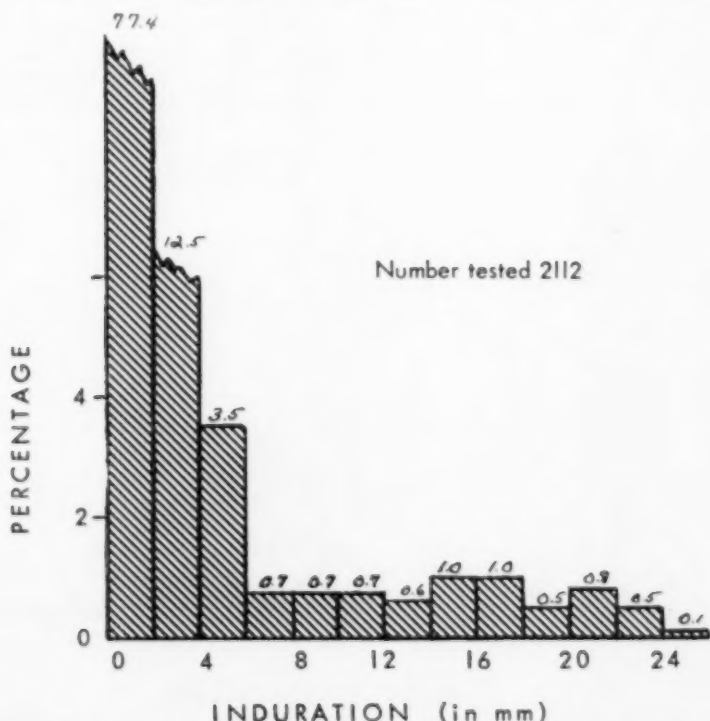


FIGURE 2: Frequency distribution by size of reaction to 5 TU of PPD-S, among high school students in Whitfield-Murray Counties, Georgia.

nonspecific reactions. Thus, as indicated in a recent publication,<sup>13</sup> a fair estimate of the prevalence of tuberculous infection can be made by using a criterion of 10 mm. or more for a positive reaction.

The percentage of positive tuberculin reactors, so defined, is given in table 2 by school (and sex) according to residence and age. Lifetime residents of the community include only those persons who were born in, and had never lived outside of, Whitfield or Murray Counties or any of the 10 adjoining counties (see map, fig. 1). Almost three-fourths of the students, 1,542 of the 2,112, could be classified as lifetime residents. The average percentage of tuberculin reactors among the white students was low, less than 5 per cent, with only minor variations from school to school and by sex, age and residence in the community.

The prevalence of infection among Negro students, although less than 100 were tested, appears to be several times higher than among white students.

#### *Histoplasmin sensitivity*

Reactions to histoplasmin are distributed according to size in figure 3. About 60 per cent of the reactions were recorded as 0 or 1 mm., followed by an abrupt drop to 6.5 per cent for reactions of 2 or 3 mm., 1.4 per cent for 4 or 5 mm., and only 1.1 per cent for reactions of 6 or 7 mm. Thereafter, with increasing size of reaction, the frequencies rose to reach a maximum of 7.1 per cent at 12-15 mm. and then tapered off. The distribution is bimodal in form, with the right-hand segment resembling the normal probability frequency curve and separating itself from the

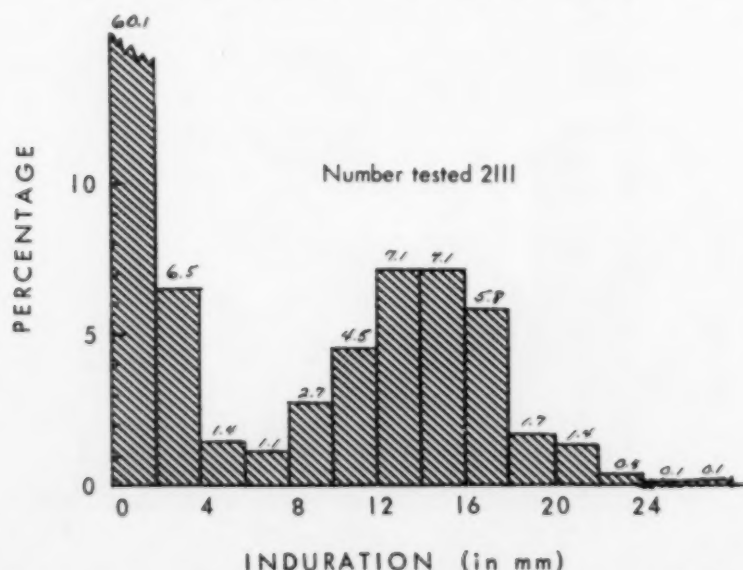


FIGURE 3: Frequency distribution by size of reaction to histoplasmin (H-42), among high school students in Whitfield-Murray Counties, Georgia.

left-hand segment in the neighborhood of 6 mm. As the two doses of histoplasmin used in the present study produced only small differences in the sizes of the reactions,<sup>14</sup> results for both doses have been combined.

From the form of the distribution, it may be inferred that most of the reactions measuring less than 6 mm. belong to the negative (uninfected) group and most of the larger reactions belong to the positive (infected) group. The two groups overlap to some degree in the range of about 4 to 9 mm.

The percentage of students with positive histoplasmin reactions (6 mm. or more) is given in table 3 for each school and, within each school, by sex, age group and residence in the community. For students in the four rural schools, the frequency of positive reactors ranged from about 19 to 25 per cent, with an average of nearly 22 per cent. The frequencies were more than twice as high for students attending the two urban schools in Dalton—55 per cent for the white students at Dalton High and 56 per cent for the Negro students at Emory High.

In almost all instances, somewhat higher frequencies of positive reactors were found among boys than girls, among older than younger students within the six-year age span, and for lifetime as compared with non-lifetime residents. The apparent reversal in the frequency with age among

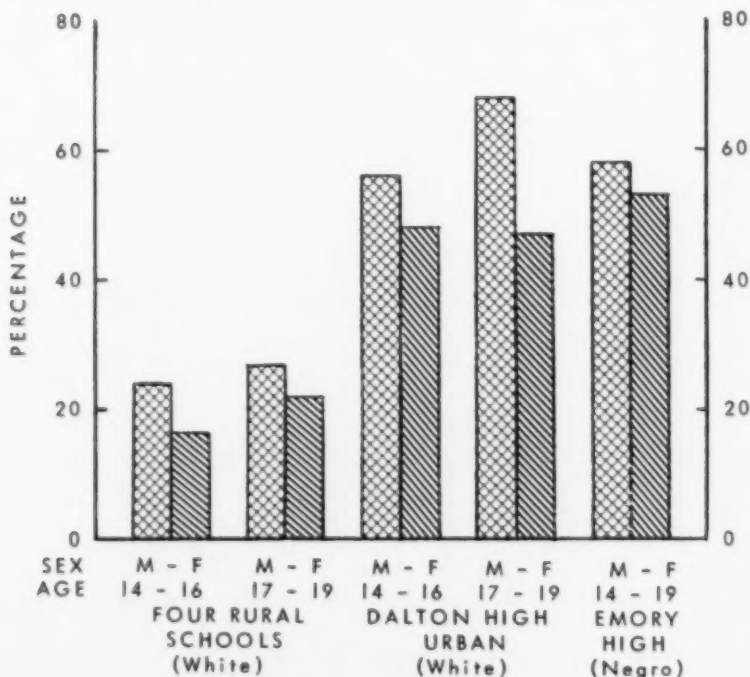


FIGURE 4: Percentage of histoplasmin reactions 6 mm. or more among high school students grouped according to age, sex, race, and rural or urban residence in Whitfield-Murray Counties, Georgia.



TABLE III

NUMBER AND PER CENT OF STUDENTS WITH HISTOPLASMIN REACTIONS OF 6 MM. OR MORE, AMONG 14-16 AND 17-19 YEAR AGE GROUPS, BY SCHOOL AND SEX, ACCORDING TO RESIDENCE IN WHITFIELD-MURRAY COUNTIES, GEORGIA

School and Sex	Lifetime and Non-Lifetime Residence										Lifetime Residence			
	All Ages					14-16 Years					17-19 Years			
	No. Tested	Reactions 6 Mm. or More		Reactions 6 Mm. or More		Reactions 6 Mm. or More		No. Tested	Reactions 6 Mm. or More		No. Tested	Reactions 6 Mm. or More		
		No.	Per Cent	No.	Per Cent	No.	Per Cent		No.	Per Cent		No.	Per Cent	
MURRAY	401	77	19.2	212	33	15.6	189	44	23.3	335	64	19.1		
Male	177	34	19.2	93	16	17.2	84	18	21.4	147	29	19.7		
Female	224	43	19.2	119	17	14.3	105	26	24.8	188	35	18.6		
NORTH WHITFIELD	486	109	22.4	287	60	20.9	199	49	24.6	359	73	20.3		
Male	214	66	30.8	117	38	32.5	97	28	28.9	155	47	30.3		
Female	272	43	15.8	170	22	12.9	102	21	20.6	204	26	12.7		
VALLEY POINT	375	81	21.6	264	52	19.7	111	29	26.1	290	63	21.7		
Male	166	42	25.3	125	28	22.4	41	14	34.1	123	34	27.6		
Female	209	39	18.7	139	24	17.3	70	15	21.4	167	29	17.4		
WESTSIDE	192	48	25.0	131	33	25.2	61	15	24.6	134	35	26.1		
Male	87	21	24.1	54	12	22.2	33	9	27.3	66	16	24.2		
Female	105	27	25.7	77	21	27.3	28	6	21.4	68	19	27.9		
TOTAL (White Rural)	1,454	315	21.7	894	178	19.9	560	137	24.5	1,118	235	21.0		
Male	644	163	25.3	389	94	24.2	255	69	27.1	491	126	25.7		
Female	810	152	18.8	505	84	16.6	305	68	22.3	627	109	17.4		
DALTON (White Urban)	559	308	55.1	285	149	52.3	273	159	58.2	344	202	58.7		
Male	284	177	62.3	140	79	56.4	144	98	68.1	171	113	66.1		
Female	275	131	47.6	145	70	48.3	129	61	47.3	173	89	51.4		
EMORY (Negro)	98	55	56.1	63	40	63.5	35	15	42.9	79	47	59.5		
Male	51	30	58.8	27	19	70.4	24	11	45.8	43	27	62.8		
Female	47	25	53.2	36	21	58.3	11	4	36.4	36	20	55.6		

Negro students may be ascribed to random variations in a small sample.

Figure 4 presents a summary picture of the histoplasmin test results. The high frequencies of positive reactors in the two urban schools are contrasted with the much lower frequencies in the four rural schools. The figure brings out the slightly higher proportion of reactors among boys than girls—a finding consistent with reports from other communities.<sup>1, 6, 16, 17</sup>

#### *Coccidioidin sensitivity*

Coccidioidomycosis has not been reported, so far as we know, in a native resident of northwestern Georgia; and studies of coccidioidin sen-

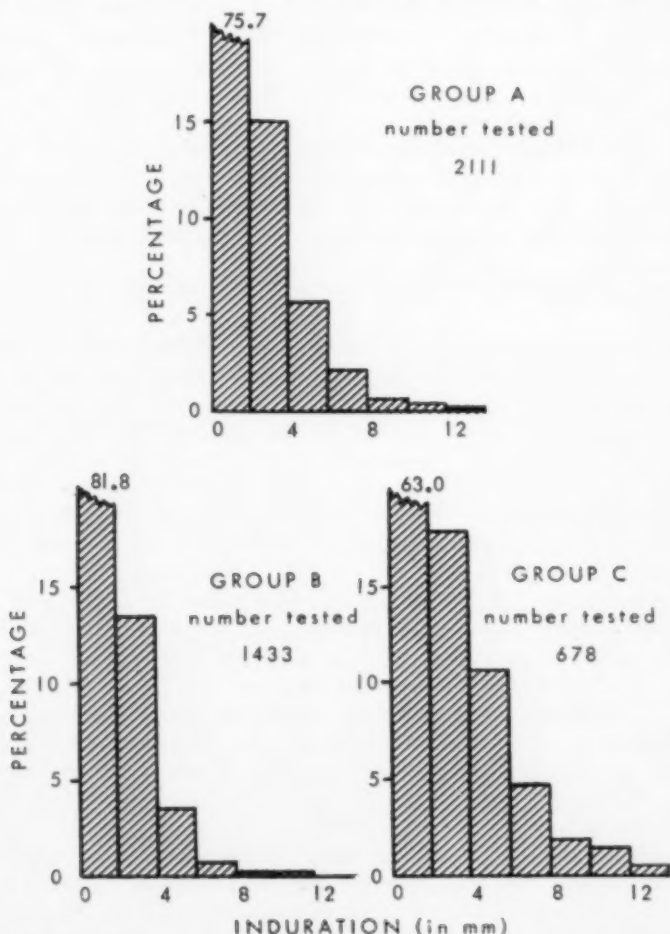


FIGURE 5: Frequency distribution by size of reaction to coccidioidin (C-24) among all high school students (A), those with a histoplasmin reaction of less than 6 mm. (B) and those with a histoplasmin reaction of 6 mm. or more (C) in Whitfield-Murray Counties, Georgia.

sitivity indicate that the endemic area of *Coccidioides* infection in the United States is limited to the southwest.<sup>18-19</sup> The present survey thus offered an opportunity to study the nature and frequency of nonspecific (heterologous) sensitivity to coccidioidin in a locality far from the *Coccidioides* endemic area.

The frequency distribution by size of reaction to coccidioidin is given in the upper part of figure 5 for the entire study population and, in the lower section, for those with histoplasmin reactions of less than 6 mm. (left) and those with histoplasmin reactions of 6 mm. or more (right). The distribution for the total group shows that all but a very few of the reactions were recorded as zero or only a few millimeters in diameter: the frequency of reactions 6 mm. or more was 3.4 per cent.

Because of the clear point of separation at 6 mm. for histoplasmin reactions (see fig. 3), students with reactions of less than 6 mm. probably represent a fairly "pure" group of persons not infected with histoplasma. Coccidioidin reactions in this group, shown in the lower left section of figure 5, can not be regarded as cross-reactions owing to histoplasma infection. They must, with few exceptions (discussed below), represent the kind of reactions that can be expected in a group free of infection with *coccidioides* and histoplasma. Only 1 per cent of the reactions measure more than 5 mm. and only 0.2 per cent measure more than 7 mm.

The distribution of coccidioidin reactions for the group of students who probably have been infected with histoplasma, shown in the lower right section of the figure, provides information about the size and frequency of nonspecific (cross) reactions to coccidioidin in persons sensitized by histoplasma infection. Comparison of this distribution with the one at the left indicates that at least some of the 2 and 3 mm. reactions must be cross reactions; and a substantial proportion of the 4 and 5 mm. reactions and almost all of the reactions of 6 mm. or more must be cross reactions.

Although the details are not given, results for boys and girls were analyzed separately. Among the 370 boys with positive reactions (6 mm. or more) to histoplasmin, coccidioidin reactions of 4 mm. or more were found in 85 (23.0 per cent), as compared with 45 of the 309 girls (14.6 per cent). A difference between the sexes was also found for students with negative reactions (less than 6 mm.) to histoplasmin: for boys the frequency of coccidioidin reactions of 4 mm. or more was 6.4 per cent (39 out of 609), for girls it was 3.3 per cent (27 out of 824). In both instances the differences are statistically significant.

As shown in table 4, 16 of the students had coccidioidin reactions of 10 mm. or more. The two with the largest reactions (17 mm. and 20 mm.) had lived in the southwest and probably acquired an infection with *Coccidioides*. A few others may also have lived in the southwest but forgot to say so when asked for their residence history, or they may have merely visited or lived for a short period in the *coccidioides* endemic area, a fact that would not have been brought out in obtaining the resi-

dence history. But the remainder may simply be highly sensitive persons with fairly strong cross-reactions, as in all but 2 instances the reactions to coccidioidin were smaller than to histoplasmin.

There is no evidence from this material that *Coccidioides* infection is indigenous to northwestern Georgia.

#### *X-ray findings*

The 70 mm. x-ray films for 87 of the 2,111 students were interpreted independently by two readers as showing either pulmonary calcification or infiltration. In 73 instances both readings indicated the presence of calcifications; in 12 instances one indicated calcification and the other an infiltration; and in 2 instances both readings agreed on the presence of an infiltration.

All but six of the 87 students with pulmonary findings reacted to histoplasmin, as shown in table 5. Only three of the 87 reacted to tuberculin, 2 of whom were histoplasmin non-reactors, the third had a histoplasmin reaction of 17 mm. Two had coccidioidin reactions measuring 11 mm. and both of them had histoplasmin reactions of 15 mm. As both were lifetime residents of the community, having been born and lived all their

TABLE IV  
CORRELATION OF SIZES OF REACTIONS TO HISTOPLASMIN AND  
COCCIDIOIDIN AMONG HIGH SCHOOL STUDENTS IN  
WHITFIELD-MURRAY COUNTIES, GEORGIA

Reaction to Histoplasmin in millimeters of induration	Reaction to Coccidioidin in millimeters of induration									Total
		0-1	2-3	4-5	6-7	8-9	10-11	12-13	14 or More	
	0 - 1	1047	160	45	10	1	2	....	1 (17)†	1266
	2 - 3	100	32	4	2	....	....	....	....	138
	4 - 5	25	3	1	....	....	....	....	....	29
	6 - 7	14	4	4	1	....	....	....	....	23
	8 - 9	47	8	1	1	....	....	....	1 (20)‡	58
	10 - 11	60	20	11	2	1	1	....	....	95
	12 - 13	92	30	13	8	6	1	....	....	150
	14 - 15	87	28	22	5	2	5	1	....	150
16 - 17	77	17	15	7	3	2	1	....	122	
18 - 19	28	4	2	2	....	....	....	....	36	
20 - 21	11	9	3	6	1	....	....	....	30	
22 - 23	7	1	1	....	....	....	....	....	9	
24 - 25	2	....	....	....	....	1	....	....	3	
26 - 27	2	....	....	....	....	....	....	....	2	
Total	1599	316	122	44	14	12	2	2	2111	

† 5 years residence in California.

‡ 2 years residence in Texas.

lives in Whitfield County, their reactions to coccidioidin were probably nonspecific and the pulmonary calcifications a result of histoplasma infection.

Analysis of the frequency of calcifications among histoplasmin reactors of 6 mm. or more revealed an unexpected statistically significant difference between the sexes: the calcification rate was 15.1 per cent among boys and only 8.1 per cent among girls.

Thus, the pulmonary findings can be attributed to histoplasmosis in all but seven of the 87 instances. In two of those seven cases the findings can probably be ascribed to tuberculosis and in both instances the two readers identified the same lesions, described as infiltrations in the right upper lung field. In one other case the student reacted to both tuberculin and histoplasmin, so the findings could be due to either infection. And in the four remaining cases, the etiology of the lesion is unknown, as the students did not react to any of the three skin tests.

TABLE V  
FREQUENCY OF PULMONARY CALCIFICATIONS, INFILTRATIONS BY  
SIZE OF REACTION TO HISTOPLASMIN, AMONG HIGH SCHOOL  
STUDENTS IN WHITFIELD-MURRAY COUNTIES, GEORGIA

Histoplasmin Reaction (Millimeters)	Total		Calc./Infilt.*	
	Number	Per Cent	Number	Per Cent
0 - 1	1266	60.1	6**	0.5
2 - 3	138	6.5	....	....
4 - 5	29	1.4	....	....
6 - 7	23	1.1	4	9.9
8 - 9	58	2.7	4	
10 - 11	95	4.5	9	14.7
12 - 13	150	7.1	27	
14 - 15	150	7.1	19†	11.4
16 - 17	122	5.8	12‡	
18 - 19	36	1.7	4	7.5
20 - 21	30	1.4	2	
22 - 23	9	0.4	....	
24 - 25	3	0.1	....	
26 - 27	2	0.1	....	
Total	2111	100.0	87	4.1
Reactions less than 6 mm.	1433	67.9	6	0.4
Reactions 6 mm. or more	678	32.1	81	11.9

\*Two readers read the 70 mm. films independently as showing calcification or infiltration.

\*\*Includes 2 persons with tuberculin reactions of 20 mm. and 21 mm.

†Includes 2 persons with coccidioidin reactions of 11 mm. (both lifetime residents of Whitfield County).

‡Includes 1 person with a tuberculin reaction of 18 mm.

*Discussion*

A striking finding in the present survey is the reversal of the usual urban-rural relation in prevalence of histoplasmin sensitivity. Prior and Allen<sup>15</sup> reported some 10 years ago that the histoplasmin reactor rate among Ohio University students was appreciably higher for those coming from farms than from cities, and later reports from other areas<sup>3, 5, 16</sup> have been in substantial agreement with their findings. The most recent contribution to the subject, a study by Furcolow and Ney<sup>20</sup> of Kansas City school children, has led those authors to conclude that there is "a strong positive relationship . . . between amount of contact with farms and the prevalence of positive histoplasmin skin tests."

In the present survey the high frequency of histoplasmin reactors in students attending the two urban schools and the much lower frequency of reactors in the four rural schools points directly to a source of infection within the urban area of Dalton to which both Negro and white children appear to be exposed about equally. We would postulate further that contact with a source in Dalton could account for many, if not most, of the histoplasmin reactors found among the rural residents. This indication of a potent source of infection in an urban rather than rural area is of considerable epidemiological interest, as it may represent a unique situation which in no way invalidates the evidence that sources of infection are ordinarily found in rural areas.

Analysis of the sizes of the histoplasmin reactions in the present material, as compared with the sizes of reactions found in other areas where *Coccidioides* and other fungi cause nonspecific (heterologous) sensitization to histoplasmin,<sup>19, 21, 22</sup> indicates that histoplasmin sensitivity in the Whitfield-Murray area is specific for infection with histoplasma. The high correlation between pulmonary calcification and histoplasmin sensitivity further supports that interpretation. It also suggests that the source of infection in the community has been present for some years, as it takes several years for calcium to replace a pulmonary infiltration.

Most of the coccidioidin sensitivity in lifetime residents of the area is interpreted as nonspecific. The coccidioidin reactions were of small average size and were generally found in persons who reacted to histoplasmin. There was, however, a significantly higher frequency of nonspecific coccidioidin reactions in boys than in girls. As far as we know, this is a new and unexpected finding; further study of it should lead to a better understanding of the nature and significance of nonspecific sensitivity to the fungus antigens.

Tuberculin sensitivity showed a frequency of about 5 per cent in the white high school students—a prevalence only slightly higher than that reported for young people in various other communities.<sup>1, 2, 5, 7, 9</sup> An average prevalence of 5 per cent at 16 to 17 years of age corresponds to an average infection rate of a little more than 3 per 1,000 per year. If, as seems likely, the infection rate has dropped in this community, as it has in most communities, during the lifetime of these young people, many



of them probably got their tuberculous infection in early childhood. In other words, the infection rate at the present time may be considerably lower than 3 per 1,000 per year.

From a medical and public health standpoint, the present survey reveals that there may be four or five students in the high school age population who have had a coccidioidal infection, somewhat more than 100 who have had a tuberculous infection and at least 700 who have had a histoplasma infection. Clearly, histoplasmosis is an infection to be reckoned with in this community. Abnormalities in the chest x-ray films of these young persons are far more often a result of histoplasma than tuberculous infection.

As an immediate consequence of the survey, a systematic search has been started through the Health Department's tuberculosis case register for persons with histoplasmosis misdiagnosed as tuberculosis. Skin testing with histoplasmin in addition to tuberculin has also been instituted in the clinic work. Tuberculosis is of course still the main problem, but the frequency of tuberculin reactors among the high school students indicates that the infection rate has been relatively low during the last 15 years and an energetic campaign to find and eliminate the infectious cases in the community should result in a further reduction in the rates.

#### SUMMARY

A skin-testing survey with histoplasmin, coccidioidin and tuberculin, supplemented with 70 mm. chest photofluorograms, was carried out among students attending the six public high schools in Whitfield and Murray Counties, Georgia. About 90 per cent of the total estimated enrollment of 2,400 participated in the survey.

Results showed a striking reversal of the usual rural-urban pattern of prevalence of sensitivity to histoplasmin. Students living in the urban area of Dalton had a reactor rate of 55 per cent as compared with a rate of 22 per cent for those living in the rural areas. Pulmonary calcifications were found in about 12 per cent of the histoplasmin reactors. Analysis of the findings lead directly to the hypothesis that there is a source of histoplasma infection within the City of Dalton which has been present for at least several years.

About 5 per cent of the white students had reactions interpreted as positive to the 5 TU test with PPD, with only small variations around that average from school to school and between boys and girls. The rates were slightly higher for the older as compared with the younger students within the six-year age span 14 to 19 years.

Coccidioidin reactions, which were of small average size, were interpreted as nonspecific (or cross) reactions owing to histoplasma infection.

#### RESUMEN

Se llevó a cabo una investigación con las pruebas cutáneas de histoplasmina, coccidioidina y tuberculina entre los estudiantes de seis escuelas



secundarias públicas completándose con fotofluorografías de 70 mm. en los condados de Whitfield y Murray en Georgia.

Aproximadamente 90 por ciento del total de los 2,400 estudiantes participaron en la investigación.

Los resultados demostraron una notable inversión de la prevalencia de sensibilidad de la tuberculina en comparación con la habitual relación de la población urbana a la rural.

Los estudiantes que viven en el área urbana de Dalton, tienen una proporción de reactores de 55 por ciento comparada con un 22 por ciento de los que viven en el área rural.

Se encontraron calcificaciones como en 12 por ciento de los reactores a la histoplasmina. El análisis de los resultados condujo a la hipótesis de que existe una fuente de infección de histoplasma dentro de la ciudad de Dalton que ha estado ahí por lo menos varios años.

Aproximadamente 5 por ciento de los estudiantes de raza blanca tuvieron reacciones positivas a 5 TU con PPD con sólo pequeñas variantes entre las diversas escuelas y entre muchachos y señoritas. Las proporciones fueron ligeramente mayores para los de más edad comparándose con los menores dentro del término de seis años entre los 14 y 19 años.

Las reacciones a la coccidioidina, que en general fueron de tamaño pequeño se interpretaron como no específicas debidas a la infección de histoplasmosis.

#### RESUME

Un contrôle des réactions cutanées à l'histoplasmine, à la coccidioidine et à la tuberculine, associé à des radiophotographies du thorax de 70 mm. fut pratiqué chez les étudiants fréquentant les six facultés publiques des Comtés de Whitfield et Murray, en Géorgie. Environ 90% de l'effectif total que avait été estimé à 2.400 participèrent au contrôle.

Les résultats montrèrent un contraste frappant entre les tracés habituels rural et urbain de la sensibilité à l'histoplasmine. Chez les étudiants vivant dans la zone urbaine de Dalton, on constata un taux de réaction de 55%, alors que le taux de ceux qui vivent dans les zones rurales était de 22%. Des calcifications pulmonaires furent trouvées chez 12% des individus réagissant à l'histoplasmine. L'analyse de ces constatations entraîne directement à l'hypothèse qu'il y a une source d'infection qui existe depuis au moins quelques ans dans la cité de Dalton.

Environ 5% des étudiants de race blanche fournirent des réactions interprétées comme positives à 5 unités de tuberculine P.P.D., avec seulement de légères variations d'une école à l'autre et selon que l'on s'adresse aux garçons ou aux filles. Les taux furent légèrement plus élevés pour les étudiants les plus âgés, la comparaison portant sur les étudiants dont l'âge variait de 14 à 19 ans.

Les réactions à la coccidioidine de dimension généralement réduite, furent interprétées comme non spécifiques, compte tenu de l'infection par l'histoplasma.

## ZUSAMMENFASSUNG

Eine Untersuchungsreihe mit Hautempfindlichkeitsprüfungen auf Histoplasmin Coccidioidin und Tuberkulin, ergänzt durch 70 mm. Thorax-Schirmbilder, wurde unter den Schülern durchgeführt, die sechs Staatlichen höheren Lehranstalten in den Kreisen Whitefield und Murray im Staate Georgia angehörten. Ungefähr 90% der gesamten auf 2400 berechneten Angehörigen nahmen an der Untersuchung teil.

Die Ergebnisse zeigten eine auffallende Umkehr der gewöhnlichen Verhältnisse von Land zu Stadt bei dem Auftreten der Histoplasminempfindlichkeit, Schüler, die im städtischen Bereich von Dalton lebten, hatten einen Prozentsatz von 55% positiven Reaktionen im Verhältnis zu einer Zahl von 22% bei denjenigen, die auf dem Lande lebten. Pulmonale Verkalkungen wurden in ungefähr 12% der auf Histoplasmin reagierenden Personen gefunden. Eine Auswertung der Befunde führte unmittelbar zu der Hypothese, dass in der Stadt Dalton eine Quelle für eine Infektion mit Histoplasma besteht, die seit mindestens mehreren Jahren existiert.

Ungefähr 5% der weissen Schüler hatten Reaktionen, die als positiv bei dem Test mit 5 Tuberkulineinheiten mit PPD gedeutet wurden und mit nur geringen Abweichungen von diesem Durchschnitt von Schule zu Schule und zwischen Knaben und Mädchen. Die Zahlen lagen ein wenig höher bei den älteren im Vergleich zu den jüngeren Schülern innerhalb der 6-Jahres-Spanne von 14 19 Jahren.

Coccidioidin-Reaktionen, die durchschnittlich von geringer Grösse waren, wurden als unspezifische (oder Kreuz-) Reaktionen gedeutet infolge Infektion mit Histoplasma.

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## Pulmonary Resection for Tuberculosis Under Protection of Viomycin, Promizole and Pyrazinamide

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### *Introduction*

The addition of chemotherapeutic agents to the armamentarium for the treatment of tuberculosis has been of inestimable value in decreasing morbidity and mortality. It has been largely responsible for the great progress in resectional pulmonary surgery, which otherwise usually would have been denied the patient. As is well known, however, bacterial resistance to the antimicrobial drugs has developed in a sizable tuberculous population and this may present an ever-increasing problem in the future treatment and retreatment of tuberculosis. Unless proper use of specific drug combinations is effected at all times to meet the particular problem at hand, the effectiveness of the drugs will be lost in a significant percentage of cases. Many workers are making great strides toward preventing resistance by application of carefully selected treatment schedules and well-timed definitive surgery.

At present, a large backlog of patients is developing with open positive lesions harboring tubercle bacilli either proved or presumptively resistant to PAS, INAH and streptomycin. These are posing a special problem and require most thoughtful handling by the specialist team.

Many reports now attest to the increased percentage of complications that occur whenever resection is attempted in the presence of tubercle bacilli resistant to the antimicrobial therapy. Coleman and Bunch<sup>1</sup> early pointed out the increased incidence of major complications, especially bronchopleural fistulae, following surgery in patients with streptomycin resistant strains. Murphy<sup>2</sup> reported satisfactory results in only 77.6 per cent of operations for cavitary lesions as compared to 94.7 per cent where closed lesions had been resected. Where sputa were positive, only 82.8 per cent of the patients had good results as compared with 94.4 per cent when the sputa were negative.

Holland, Bell and Welles<sup>3</sup> found similar results in 75 patients with open positive lesions. Of an original chemotherapy susceptible group, there was only one major complication in 19 resections as contrasted with five complications in nine resections in the presence of bacterial resistance. The retreatment group had three major complications in 22 resections if the bacilli were susceptible, but with resistant organisms there were nine major complications in 33 resections. Overall favorable results were achieved in

\*Read by title at the 23rd Annual Meeting, American College of Chest Physicians, New York City, May 29-June 2, 1957.

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95.5 per cent of the susceptible group but in only 71 per cent of the resistant group. They found that late tuberculous complications occurred in one-third of their resistant cases, a morbidity reminiscent of the pre-drug era. Of their total 17 cases with postoperative parenchymal reactivation in over 500 resections, 15 had resistant tubercle bacilli. In eight patients in whom resistance was not suspected, parenchymal reactivation followed promptly after segmental excision. As a result, they prefer to do lobectomies rather than segmental resections in the presence of resistance.

Lees,<sup>4</sup> in reviewing more than 300 resections during the recent period of antimicrobial therapy, found that over 85 per cent of the complications had occurred in those patients with preoperative positive sputa. Hughes,<sup>5</sup> in an experience of approximately 500 resections for tuberculosis, noted a tremendous increase in the percentage of complications when the tubercle bacilli were resistant.

Robinson, Jones, Meyer, and Reding<sup>6</sup> reported their experience with surgery in 1363 tuberculous patients. Of the nine with resistant bacteria, one died early and three late and all nine developed serious complications. Wareham and co-workers<sup>7</sup> found a marked increase of persistent postoperative pleural spaces in the presence of drug resistant bacilli. Of 71 resections in negative sputa cases, only three developed symptomatic pleural air spaces and all were cured by an ancillary surgical procedure; however, of 33 positive patients, 10 developed symptomatic air spaces which responded only poorly to subsequent surgical intervention. Of these, three are dead, five remained active, and only two have been cured.

Contrary to this extensive experience, Falk and Tucker<sup>8</sup> reported, in 1954, that bacterial resistance had little or no effect upon relapse or failure. Likewise, Kukral<sup>9</sup> and coauthors state that, in the patient with isoniazid resistant catalase negative tubercle bacilli, the risk of serious postoperative spread of disease is minimal or absent.

Recently, sputum positive and resistant cases have been subjected to definitive pulmonary resection with the aid and coverage of ancillary drugs. Walkup and coauthors,<sup>10</sup> in 1952, reported the adjunctive use of viomycin in pulmonary surgery. Three grams of the drug were given daily for 21 days in a series of 32 resections. This regimen was of questionable value due to toxicity and a high incidence of postresection complications. They suggested reducing the dosage and combining viomycin with other drugs. In 1954, Murphy<sup>11</sup> recorded his experience with 13 patients in whom pulmonary resection was performed under PZA protection. Though nine of the patients were resistant to streptomycin, the only complication was one postoperative bronchopleural fistula.

Holland, Bell and Welles,<sup>3</sup> in 1955, reported resections under viomycin and terramycin protection on nine patients with cavitory lesions containing organisms resistant to streptomycin, INAH and PAS. As three of these nine had major complications, they did not consider this combination promising.

McLean and Benson,<sup>12</sup> in 1956, reported their experience with 24 patients considered "treatment failures" who were subjected to a viomycin-pyrazinamide program which lasted from two to 10 months. Viomycin was given in doses of one gram at 12-hour intervals two times per week and PZA was given in doses of one gram three times daily. About 50 per cent of these cases demonstrated some type of mild toxic reaction with a smaller percentage requiring discontinuance of the drug. In four patients with positive sputa and drug resistance, five pulmonary resections were performed early in the course of PZA-viomycin therapy (third through the eighth week). Two of the cases became inactive, one became sputum negative with stable "open negative" status, and the fourth relapsed on the fifth month after pneumonectomy for a destroyed lung. They recommend this combination for necessary surgery requiring additional drug protection and for acute exacerbations to minimize the extent of spread and necrosis.

It is the purpose of this study to analyze the surgical experience of 32 patients, with open positive lesions and bacillary resistance to streptomycin, INAH and PAS, who had resections under protection of viomycin-promizole and viomycin-PZA combinations.

### *Drugs*

Viomycin,<sup>13</sup> produced by an actinomycete, although less active than streptomycin or isoniazid, is definitely more potent than PAS. Although toxic manifestations occur when viomycin is utilized daily, experience has indicated that, when used intermittently at two grams intramuscularly twice weekly, untoward reactions occur rarely and are generally mild.<sup>14</sup> Toxic manifestations may consist of auditory acuity loss, electrolyte imbalance, renal toxicity and skin eruptions.<sup>15</sup>

Pyrazinamide<sup>16</sup> is a potent synthetic antituberculosis agent, but when employed alone microbial resistance develops within a period of six to eight weeks.<sup>17</sup> Its use has been limited principally to seriously ill hospitalized patients with tuberculosis unresponsive to other agents. Four to 15 per cent of patients develop toxic manifestations,<sup>18</sup> particularly hepatitis and nonspecific symptoms including anorexia, nausea, vomiting, arthralgias, dysuria and fever. Pyrazinamide is usually given in doses not greater than 35 milligrams per kilogram a day and on the average of 500 milligrams four times daily.

Promizole, a synthetic heterocyclic sulfone compound,<sup>19</sup> is a relatively nontoxic agent which may be employed over a prolonged period.<sup>20-21</sup> Its most extensive uses have been in the treatment of miliary tuberculosis<sup>22</sup> and as a valuable adjunct to streptomycin for tuberculosis meningitis.<sup>23</sup> A daily dosage of one gram is started and increased to maintain a blood level of two to three milligrams per cent. Even at best, however, it must be classified as one of the weakest of present day tuberculostatic drugs. Its use in combination with viomycin for surgical protection in resistant open positive lesions has not been described heretofore.



### *Material*

The present study is a review of 35 resections in 32 patients, all of whom had open positive lesions with bacilli proved or presumptively resistant to streptomycin, isoniazid and PAS. Each patient was placed on viomycin in combination with promizole or with pyrazinamide for a two-week period preoperatively and this regimen was continued for approximately three months postoperatively. The usual dosages administered were viomycin, two grams twice a week; promizole, one gram four times daily; and pyrazinamide, approximately 25 milligrams per kilogram or 500 milligrams four times daily. During this period, streptomycin, PAS and isoniazid in the combinations which the patients had been receiving were maintained for whatever value they might possess.

All patients were sputum positive within the six-weeks period immediately prior to surgery. The patients were classified as resistant to these three drugs if cultural growth was not diminished by 10 micrograms of streptomycin, 10 micrograms of PAS or one microgram of isoniazid. If the bacilli could not be cultured, those patients with open cavities and positive smears who had had chemotherapy for a minimum of one year were classified as presumptively resistant. Only two in this total series had total therapy of less than one year and in both of these the bacilli were proved resistant by culture. Only nine had been treated less than 18 months. The others had received intermittent drug therapy up to seven years. Thirty are retreatment cases, having had interrupted courses with two, or all three, of these drugs. Again, the two who had not had interrupted courses of treatment were proved by culture to have resistant bacilli.

The duration of total illness was likewise quite long as only 13 had had active pulmonary tuberculosis less than three years. The others ranged up to 10 years since the initial onset of active pulmonary tuberculosis. They varied in age from 18 to 60, with 18 being over 40 years of age. Seventeen had previous collapse therapy, 10 having pneumoperitoneum; six, pneumothorax; and seven were thoracoplasty failures, one having had bilateral thoracoplasties. One had a previous Monaldi procedure.

Classification of disease by x-ray film standards on admission showed 28 had far advanced disease with four moderately advanced. Classification by the last preoperative x-ray film showed 22 still remained far advanced and 10 moderately advanced. No minimal lesion was encountered which met the criteria for inclusion in this particular series. The contralateral lung was considered clear or minimal in only 16 cases, while 12 showed definite cavitation.

The resections were of considerable magnitude in this group as 10 had pneumonectomies, 11 lobectomies, eight lobectomy plus segmental procedures and only three patients' resections were limited to segmental excisions, one of these being bilateral.

Those with bilateral surgery had the following resections: 1a) left upper lobe and b) apical posterior segments right upper lobe, 2a) right upper lobe and superior division right lower lobe and b) apical posterior



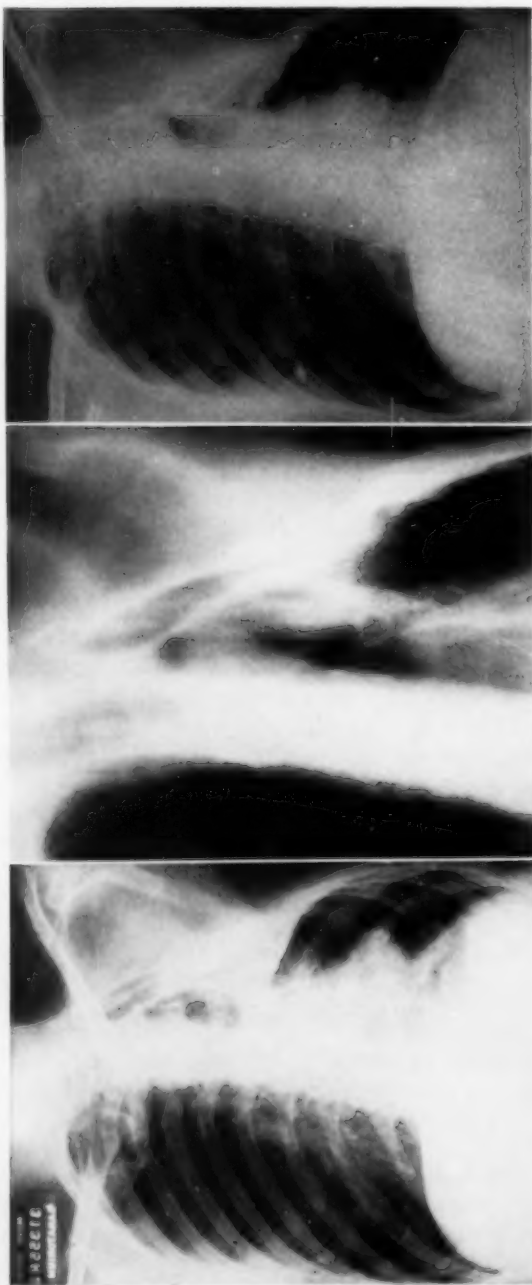


FIGURE 1A

FIGURE 1B

FIGURE 1C

FIGURE 1: B. G., 54 year old white man. Onset of pulmonary tuberculosis 1947. Thoracoplasty, 1949. Intermittent streptomycin and PAS since 1949 and INAH since 1953. Resection of left upper lobe and anteromedial basilar segment left lower lobe on March 1, 1956.—*Figure 1A*. Preoperative PA roentgenogram. Note the consolidation opposite the apex of the heart.—*Figure 1B*. Preoperative laminogram showing large cavity beneath thoracoplasty.—*Figure 1C*. PA chest one year postoperatively.

segment left upper lobe, 3a) apical posterior segment left upper lobe and b) apical posterior segments right upper lobe. Another had a left decortication and resection of the right upper lobe and superior division right lower lobe.

*Indications for surgery.* In each case the residual lesion was already a collapse therapy failure (Fig. 1) or thought inappropriate for collapse therapy. In each instance there was an open cavity, often with evidence of bronchiectasis or bronchostenosis. Nodular and fibrocaseous disease was present in virtually every case. The lobes and lungs removed were usually carnified (Fig. 2) or destroyed.

*Operative Findings.* The operations presented unusual technical difficulties due to severe degrees of hilar fibrosis and multiple enlarged and adherent lymph nodes surrounding the vessels and compressing the bronchi. Operative hemorrhage occurred in four cases due to injury to the pulmonary arteries. In each case it was possible to control this and complete the contemplated procedure.

### Results

There were four deaths in this series, none of which was related to the resistant bacilli or drug status. One patient had a massive pulmonary embolus while on the operating table. A second died on the 20th post-operative day from pulmonary emboli proved by autopsy. The third death occurred from pulmonary circulatory insufficiency six days after resection of the left upper lobe and superior division of the left lower lobe and plombage thoracoplasty. At autopsy, the contralateral pulmonary artery

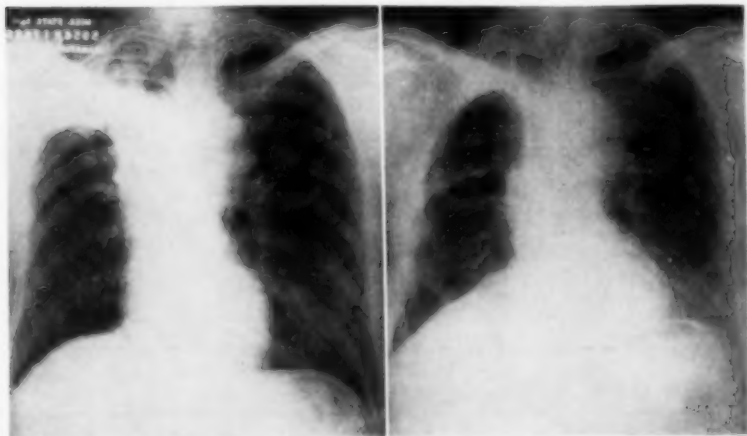


FIGURE 2A

FIGURE 2B

FIGURE 2: A. G., 51 year old white man. Onset of disease 1948. Intermittent streptomycin and PAS since 1951 and INAH since 1953. Resection of consolidated right upper lobe with 5 cm. cavity October 18, 1956.—*Figure 2A.* Preoperative PA roentgenogram chest.—*Figure 2B.* PA chest, following resection of right upper lobe and tailoring thoracoplasty. Sputa negative.

was found to be almost totally occluded by a large arteriosclerotic plaque thought to be an old organized thrombus. The fourth patient died of myocardial failure with pulmonary edema on the first day after resection of the destroyed right lung. Autopsy revealed enlargement of the heart with extensive acute "myocardosis."

There was no bronchopleural fistula, empyema or postoperative spread but two early reactivations did occur (Chart 1). One had reactivation of a small area of former disease in the contralateral base one month postoperatively which has been controlled by pneumothorax now discontinued after two and one half years. The sputa have remained consistently negative. The second had reactivation of a residual lesion in the contralateral upper lobe three weeks after pneumonectomy for a destroyed lung. One culture was positive five months following operation, but the bacteriology has been negative for the subsequent six months and the x-ray film shows continued improvement.

Of the 28 remaining patients which have been followed from six to 36 months, 26 are negative bacteriologically with stable x-ray films (Chart II). Six were treated with viomycin and promizole and five of them are classified as arrested or inactive at this time. The sixth had had bilateral plombage thoracoplasties which failed to accomplish permanent sputum conversion. The superior division of the left lower lobe was resected for a residual cavity but eight months later the sputum again became positive and the x-ray film revealed reactivation in the right lower lobe. Six months later his x-ray film shows continued clearing and his sputa are negative.

Of the 26 patients resected under viomycin and pyrazinamide protection, four are dead as noted and 21 are arrested or inactive at this time. One

CHART I  
COMPLICATIONS—TB

	Vio-Prom	Vio-PZA
Early Reactivations	0	2
Late Reactivations	1	0
Bacterial Relapse (late)	0	3 (Temporary)

CHART II  
PRESENT STATUS

	Patients	Active	Inactive	Dead Non TB
Vio-Prom	6	1	5	0
Vio-PZA	26	1	21	4
TOTAL	32	2	26	4

mentioned above required a postoperative contralateral pneumothorax for early reactivation. Three had a single positive sputum at three, four and four months respectively after operation but they have been negative for 12, 14 and 15 months respectively now with stable x-ray films shadows.

*Other Complications.* (Chart III). There was one postoperative hemothorax which was cleared successfully by enzymatic debridement. One had a temporary cardiac arrest during the operative procedure. The heart returned to normal rhythm after only a few seconds of massage and the resection was completed without further incident.

Postoperative tracheostomies were performed in six patients. In all of these, retained secretions were a major factor. In two, however, definite respiratory insufficiency was encountered which further influenced the decision for the tracheostomy. One of these patients had to be maintained on artificial respiration for six days postoperatively but has subsequently returned to an asymptomatic status except for dyspnea on moderate exertion.

*Toxicity.* Only one patient had to have viomycin discontinued because of persistent rash and itching. No severe toxic manifestation was noted to pyrazinamide but one patient had to have promizole discontinued due to recurrent rash.

#### Discussion

At this time, many patients are found to have open positive tuberculous lesions with bacilli proved or presumptively resistant to streptomycin, isoniazid and PAS. Some of the patients in our series are sanatorium failures accumulated during the developmental stages of our present concepts of antibiotic therapy and of the timing of definitive surgery. Obviously many had drug regimens completely inadequate by present day standards and the optimal time for surgery was missed. Another important factor in this regard was found to be the increasing trend toward home treatment where supervision is necessarily less complete than in sanatoria. Seventeen of the above 32 patients entered the sanatorium after resistance had already developed during treatment elsewhere.

It is our belief that this group of patients became resistant because of various mechanical obstructing factors which tended to keep cavities open. Hilar fibrosis and extensive peribronchial lymphadenopathy produced bronchiectasis, bronchostenosis, tension cavities and carnified parenchyma. These would prevent cavity closure regardless of the nature

CHART III  
COMPLICATIONS—NON TB

Hemothorax	1
Cardiac Arrest	1
Tracheostomy for Secretions	6
Respiratory Insufficiency	2

of antibiotic therapy employed and thus allow the development and persistence of resistant bacilli.

These patients offer a tremendous challenge both in evaluation and in treatment. In recent years, our goals in tuberculosis therapy have shifted from being satisfied with the development of the "good chronic" with quiescent disease to the constant striving for attainment of the inactive state. As these patients are complete medical failures, surgery is frequently attempted in desperation as the only hope for these "salvage" cases. We have utilized plombage thoracoplasties in such patients with gratifying results whenever the lesion is amenable to collapse therapy. In the many patients, however, who are already thoracoplasty failures, or who have carnified disease or advanced bronchial destruction, only resection can offer reasonable hope of success.

As noted above, resection in the face of resistant bacilli is usually accompanied by a forbidding morbidity rate. Our results of resection under the temporary umbrella of viomycin and promizole or pyrazinamide indicate that this salvage surgery can be performed without undue complications even in the presence of bacilli resistant to streptomycin, isoniazid and PAS. Due to the extensive and bilateral involvement of these cases, undoubtedly many will have poor ultimate prognoses.

We have not used promizole recently since pyrazinamide, the more potent drug, has been available at a reasonable cost. With the more recent addition of cycloserine to our armamentarium, another "sprinter" drug is available for temporary coverage. Streptovaricin has not at this time been fully evaluated for its potential role, but likewise appears promising.

In view of modern knowledge of the bacteriology of the tubercle bacillus with its predilection for early resistance to any one of the known therapeutic agents, and the delaying or prevention of this phenomenon by the combination of a second drug, there does not seem to be any logical reason for using one drug whenever two are available. In many instances, the source of the positive sputum and thus the resistant bacilli have been removed at the time of surgery. If no immediate untoward reaction occurs from spillage of resistant bacilli or from uncontrolled endobronchial disease at the level of bronchial transection, the results should be favorable as the remaining bacilli may well be sensitive to the usual drugs. In salvage cases, however, where there has been extensive and bilateral involvement, particularly with cavitation, the prognosis for good long-term results must remain guarded.

#### SUMMARY

1) An analysis is presented of the temporary protection of viomycin combined with promizole or pyrazinamide in 35 pulmonary resections in 32 patients with open positive tuberculous lesions. In each, the tubercle bacilli were proved or presumptively resistant to streptomycin, PAS, and isoniazid.

2. The failure of previous medical therapy was found to be explained by mechanical factors which would prevent cavity closure regardless of the nature or duration of medical therapy.

3) There were four deaths unrelated to drug coverage. There has been no spread, bronchopleural fistula or empyema. Two patients had early and one a late reactivation. Three additional patients demonstrated late bacteriologic relapses, but have subsequently been negative over a year. Thus, of 28 survivors followed from six to 36 months, 22 have never shown postoperative activity and 26 may now be classified as arrested or inactive.

4) Viomycin combined with either promizole or pyrazinamide appears to offer satisfactory temporary protection for excisional surgery in tuberculosis. Nonetheless, promizole has not been used since the availability of the more potent pyrazinamide.

#### RESUMEN

1. Se hace un análisis de la protección temporal que produce la Viomicina asociada al promizol o pirazinamida en 35 resecciones pulmonares realizadas en 32 enfermos con lesiones tuberculosas abiertas y bacilíferas. En cada uno se demostró que el bacilo era resistente (o se presumió que así era) a la estreptomycin, el PAS y la isoniácida.

2. El fracaso del tratamiento previo pudo explicarse por factores mecánicos que evitarían la clausura de la cavidad cualquiera que fuese la naturaleza y la duración del tratamiento médico.

3. Hubo tres defunciones sin relación con el uso de la droga. No hubo diseminaciones, fistula broncopleurale o empiema. Dos enfermos tuvieron reactivación, uno temprana y otro tardía. Dos enfermos más presentaron recaída bacteriológica tardía pero después se hicieron negativos por más de un año. Así, de 28 sobrevivientes observados de seis meses a 36 meses, 22 no han tenido actividad patológica postoperatoria y 26 se han clasificado ya como detenidos o inactivos.

4. La viomicina combinada ya sea con promizol o con pirazinamida parece ofrecer una protección temporal satisfactoria para la cirugía de excisión en entuberculosis. Sin embargo, el promizol ha dejado de usarse desde que se puede obtener un agente más potente como es la pirazinamida.

#### ZUSAMMENFASSUNG

1. Es wird eine Analyse vorgelegt über den temporären Schutz von mit Promizol oder Pyrazinamid kombinierten Viomicyn bei 35 Lungenresektionen an 32 Kranken mit offenen, positiven tuberkulösen Befunden. Bei jedem dieser Fälle waren die Tuberkelbazillen nachgewiesener Massen oder vermutlich resistent gegen Streptomycin, Pas und INH.

2. Die Erklärung für das Versagen einer vorausgegangenen internen Behandlung wurde in mechanischen Faktoren gefunden, die einen Kaverneverschluss verrinderten unbeschadet der Art und Dauer der konservativen Therapie.



3. Ohne Bezug auf den medikamentösen Schirm traten 4 Todesfälle ein. Es kam zu keiner Aussaat, inneren Fistel oder Empyem. 2 Patienten bekamen eine frühzeitige und einer späte Reaktivierung. 3 weitere Kranke erwiesen späte bakteriologische Rückfälle, waren aber anschliessend mehr als ein Jahr negativ. Demnach haben von 28 Überlebenden, deren Verlauf 6-36 Monate lang weiter verfolgt wurde, 22 zu keiner Zeit eine postoperative Aktivität an den Tag gelegt und 26 können jetzt als stillstehend oder negativ gekennzeichnet werden.

4. Viomycin in Verbindung entweder mit Promycol oder Pyrazinamid scheint einen befriedigenden temporären Schutz zu bieten für die Resektionsbehandlung bei der Tuberkulose. Nichtsdestoweniger ist Promizol nicht mehr verwandt worden, seitdem das stärker wirksame Pyrazinamid zur Verfügung steht.

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## Echinococcus Cyst of the Lung

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Since patients with echinococcus cysts of the lungs are rarely seen in the United States, this report is made to alert those interested in diseases of the chest, to include that due to *Echinococcus granulosus* in differential diagnosis of pulmonary lesions. Infestation with echinococcus is common in Iceland, parts of central Europe, Italy, Africa, South America, Australia, New Zealand, Syria, Arabia, Siberia, Turkestan, the northern part of China, Japan and the Republic of the Philippines. These areas closely parallel the theaters of operation of World War II. The incidence of disease due to echinococcus may increase in the United States because large numbers of veterans of the armed forces have served in these areas. Therefore, the diagnosis and treatment of this disease should assume greater importance than it has in the past.

The common definitive hosts are dogs, wolves, jackals, coyotes and other canidae. The usual intermediate hosts are sheep, cattle, horses, other herbivorous animals, and hogs.<sup>6</sup> The moose has also been shown to be an intermediate host.<sup>42</sup> In northern Canada and most of British Columbia, the herbivora, usually the moose or caribou, may serve as intermediate hosts.<sup>36</sup> Infestation of man is accidental and ordinarily by ova in the feces of dogs.

Infection with echinococcus in all anatomical sites and in the lungs varies geographically (Table I). The number of patients in the United States and Canada (Table II) has not approached that seen in certain other parts of the world. As near as can be determined, the total number of patients with involvement of the lungs in the United States and Canada is 166 (Table III). The patient reported by Evans<sup>15</sup> was previously described by Benson, Evans and Zuelger.<sup>7</sup> The report of Miller,<sup>36</sup> however, is surprising. Ninety-seven patients with cysts in the lungs have been found in Canada with the diagnosis having been made in the previous five years from hospital records and roentgenograms of the chest. Miller<sup>36</sup> was certain that all patients, in whom the diagnosis was made by roentgenogram had hydatid cysts. The roentgenographic shadow was characteristic, however, particularly since roentgenograms taken in successive years showed a gradual increase in size of the area of disease. Miller<sup>36</sup> was reasonably sure that a correct diagnosis was made in 90 per cent of the patients. More patients with pulmonary hydatid disease in Canada have been reported by Miller<sup>36</sup> than have been known to exist in the United States and Canada previously. The present instance makes the total number of patients reported from the United States and Canada, as far as can be determined, 167.

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Three with hydatid disease of the lungs always lived in the United States as reported by Garrett,<sup>18</sup> the first of Phillips,<sup>40</sup> and of Johnson and Twente.<sup>27</sup>

The symptoms of echinococcus disease of the lungs are few and are not pathognomonic. Generally, the patients are healthy. Early symptoms are cough, slight hemoptysis, and transient episodes of elevation of temperature. Pain in the chest is not present unless the cyst is in contact with the pleura. In a review of 478 persons with pulmonary hydatid disease in New Zealand and Australia, Waddle<sup>27</sup> reported that a latent period of years may exist between the time of infection and the appearance of any symptom. The presence of a hydatid cyst becomes suspected frequently only when a complication, such as leakage, frank rupture, or bacterial infection ensues. The cyst may rupture into a lung and the contents are coughed up or rupture into the pleural space and cause empyema.

Eosinophilia is totally unreliable in the diagnosis of echinococcus infection. Moreover, it is not present in persons with cysts which have undergone suppuration or death.

Rupture of cysts into bronchi may occur and scolices, hooklets, and pieces of the laminated membrane may be coughed up. Microscopic identification of any or all of these elements offers a positive method of diagnosis.

Three diagnostic immunological reactions have been studied at length. These include the complement fixation test, the intradermal test, and the precipitin test.

Ghedini,<sup>19</sup> in 1907, first applied the complement fixation test, or the

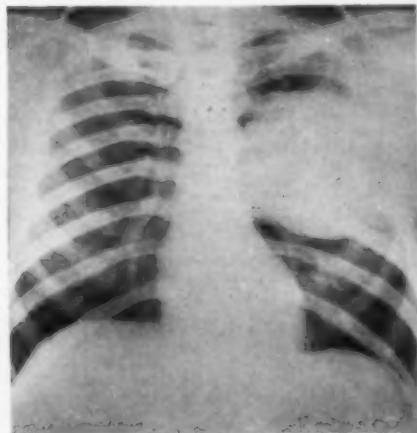


FIGURE 1



FIGURE 2

*Figure 1:* Postero-anterior roentgenogram of the chest showing homogenous mass in the upper part of the left lung on February 15, 1951.—*Figure 2:* Left lateral roentgenogram of the chest after a swallow of barium showing homogenous mass in the upper part of the left lung on February 15, 1951.

Bordet-Gengou method of serologic diagnosis, to echinococcus disease. It is a good diagnostic test. Fairley<sup>16</sup> demonstrated that a positive result depended upon whether the hydatid was alive and whether communication existed between the cyst and the host. In 45 uncomplicated cysts, where apparently a good wall was still present, a positive result was obtained in 24, (75.6 per cent) and a negative in 11, (24.4 per cent). With recent incomplete rupture of the cyst wall, 12 patients gave positive results in 11, (91.7 per cent) and a negative in one. With recent suppuration and apparent free communication between the cyst and the host, positive results were obtained in 17, (100 per cent). With death of the parasite as in two patients with chronic suppuration, three with old complete rupture, and 11 with degeneration of the parasite, negative results were

TABLE I

Authors	Year of Report	Geographical Location	Per Cent of Patients With Involvement Of Lungs
Thomas <sup>28</sup>	1894	Australia	11.5
Peiper <sup>29</sup>	1903	Germany	10.6 to 11.9
Deve <sup>18</sup>	1912	France	8.5
Fairley <sup>16</sup>	1922	Australia	13
Magath <sup>34</sup>	1921-1922	United States and Canada	5.4
Dew <sup>14</sup>	1928	Australia	12.5
Loucks <sup>30</sup>	1930	North China	6.25
Barnett <sup>2</sup>	1935	Australia	17.3
Magath <sup>35</sup>	1937	United States and Canada	6.8
Godfrey <sup>29</sup>	1937	Australia	12.5
Arce <sup>1</sup>	1941	Argentina	15
Rivas, Gobich and Mantilla <sup>31, 32</sup>	1944	Argentina	20.8
Davidson <sup>10</sup>	1944	World	10
Babcock <sup>9</sup>	1944	World	10 to 15
Strong <sup>25</sup>	1944	Endemic Areas	As much as 12
Cole <sup>11</sup>	1945	Australia and New Zealand	24.5
Barrett <sup>4</sup>	1947	Australia	25
		France	9
Miller <sup>36</sup>	1953	Canada	69
Jidejian <sup>38</sup>	1953	Lebanon	28
Susman <sup>34</sup>	1953	Australia	23
		Iceland	1.5

obtained in 100 per cent. In a series of 83 with living hydatid cysts, positive reactions were obtained in 70, (84.3 per cent), and a negative in the remainder.

The intradermal test reported by Casoni<sup>9</sup> is generally reliable although occasionally false positive reactions are obtained. Fairley and Kellaway<sup>17</sup> believe that a positive Casoni test is of diagnostic value only in patients who never had an operation for a hydatid cyst. In such patients, the response was found in about 75 per cent of those with uncomplicated or degenerating cysts. When the test was done routinely on patients in whom hydatid disease was suspected, failure to react indicated the absence of disease in at least 95 per cent. A positive result was not significant in the diagnosis of recurrent or residual cyst. In 1952, Barrett and Thomas<sup>5</sup> reported the test to be generally reliable but a positive reaction was obtained in a small group of patients with carcinoma, particularly with multiple secondary deposits. The Casoni reaction does not change quickly or certainly from positive to negative and may be positive for five or more years in a patient without persisting infestation. The reaction cannot be used as a guide to cure of any specific lesion or to indicate the presence of other hidden cysts. Rose and Culbertson,<sup>15</sup> in 1939 pointed out that the supply of fluid for use in the Casoni test is poor throughout North America thus creating difficulty in diagnosis. Four patients known to have hydatid disease gave an immediate positive reaction, however, with an antigen prepared from *Taenia pisiformis* found in the rabbit. In 1940, Rose and Culbertson<sup>16</sup> stated that the Casoni test and the complement fixation test were apparently group specific rather than species specific. Antigens made from *Cysticercus pisiformis* found in the rabbit and *Taenia taeniaformis* found in the cat could be substituted for hydatid fluid.

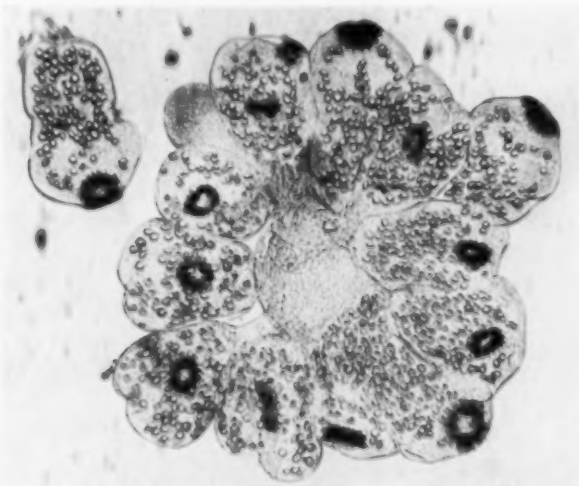


FIGURE 3: Scolices of the *Echinococcus granulosus*.

Weinberg,<sup>58</sup> in 1913, reported a study on the use of the precipitin test which is less accurate than the complement fixation test and the intradermal test. Strong,<sup>51</sup> in 1944, stated that a positive reaction with the precipitin test was obtained frequently if the antigen was good but false positive reactions occurred.

Jidejian<sup>25</sup> reported that the slow exchange of substances between the host and the contents of the cyst was responsible for the intoxication, the allergy, and the antibody formation in the host. This exchange was the cause of the eosinophilia, the Weinberg reaction, and the Casoni reaction. Positive results from all of these laboratory tests may be absent in a patient with a hydatid cyst. In addition, positive tests may become negative with a denser and less permeable cyst wall. An operation resulting in cure produces a rapid disappearance of the eosinophilia, the Casoni test, and the Weinberg reaction. Dead cysts do not produce antigen and if sufficient time has elapsed since the death of the cyst, all circulatory antibodies will disappear and all of the tests mentioned will become negative.

Aspiration for diagnosis should not be done since, if hydatid fluid containing scolices is spilled, new cysts may form. In addition, empyema may result. Aspiration should not be used in the clinical investigation of moderately large or large round lesions of the lung of unknown etiology.

A round homogenous shadow in the pulmonary parenchyma is seen in the roentgenogram of the chest of a patient with an echinococcus cyst of the lung. According to Santy, Berard, and Sournia,<sup>47</sup> when the patient is prone, has the head tilted down, and has taken a deep breath, fluoroscopy showed a transverse lengthening of the cyst as if it responded to the widening of the chest. The authors point out, however, that this is only a sign of any cyst.

Arce<sup>1</sup> has described the changes in the roentgenogram when the cyst

TABLE II

Authors	Year of Report	Geographical Location	Patients In All Anatomical Locations	Patients With Involvement of Lungs
Osler <sup>27</sup>	1892	America	61	5
Osler <sup>28</sup>	1892	United States and Canada	85	6 (Lung or Pleura)
Sommer <sup>29</sup>	1895	America	67	5
Sommer <sup>30</sup>	1896	America	100	7
Lyon <sup>31</sup>	1902	North America	241	11
Magath <sup>32</sup>	1922	North America	334	15
Magath <sup>33</sup>	1937	Canada and United States	482	32

comes into contact with a bronchus. A small amount of air may go between the membrane of the parasite and its adventitia and the air appears in the shape of a cap and gives rise to perivesicular penuma. If an opening into the membranes occurs, a part of the fluid may be expelled and air finds its way between the adventitia and the membrane and between the membrane and the remaining fluid. Two air chambers are seen to form the double arch sign described by Ivanissevich.<sup>24</sup> With marked tearing or total disintegration of the cystic membrane, a cap of air and a dull, movable horizontal shadow, which is the hydatid fluid upon which the cystic membranes float, forms the water-flower sign.

The operation for hydatid cyst has undergone considerable modification particularly since the newer advances in thoracic surgery have been made.<sup>1, 4, 5, 10, 12, 25, 29, 31, 41, 52-54, 57</sup> Surgery should be conservative, should be undertaken early to avoid complications, and should include removal of the parasite, avoidance of contamination of the wound and the pleural cavity with live hydatid elements, provision for dealing with the sac in the lung, and removal of diseased parenchyma of the lung.

Opinion as to the injection of formalin into the cyst before opening it or swabbing the cyst with formalin after evacuation varied. The chemical was used frequently, Barrett<sup>4</sup> and Waddle<sup>57</sup> pointed out that the injection of formalin was not a good procedure.

Waddle<sup>57</sup> and Barrett and Thomas<sup>5</sup> have reported large series of patients with pulmonary hydatid disease who were subjected to surgery. The



FIGURE 4



FIGURE 5

*Figure 4:* Postero-anterior roentgenogram of the chest showing the cyst with the membranes floating on the fluid on February 21, 1951.—*Figure 5:* Left lateral roentgenogram of the chest showing the cyst with membranes floating on the fluid on February 21, 1951.



type of operation varied according to the state of the disease present in the patient and the results were excellent.

*Case Report:* A 26 year old Negro, admitted to the surgical service of the hospital on February 15, 1951, had mild pain in the chest and cough, which was not productive, for about four days. The pain was sudden in onset involving the right and left sides of the chest at first but soon localizing to the left anterior thoracic region. (A history of hemoptysis, poor appetite, and loss of weight was not obtained.) He was referred for treatment when a mass in the left lung was discovered on the roentgenogram of the chest.

He had served in apparently good health in the African and in the Italian campaigns during World War II.

His temperature on admission was 99° F. The breath sounds were distant throughout both lungs and absent over the left anterior chest. Moist rales were heard in both lungs. The remainder of the physical examination was normal.

The hemoglobin was 12.1 grams per 100 cc. and the leukocyte count 6,050 per cmm. of which 68 per cent were polymorphonuclear neutrophilic leukocytes, 31 per cent lymphocytes, and 1 per cent polymorphonuclear eosinophilic leukocytes. The serologic test for syphilis was negative. Acid-fast bacilli were not found in the sputum.

A shadow of a round homogenous mass about nine cm. in diameter was seen in the upper part of the left lung on the postero-anterior roentgenogram of the chest (Figure 1). An ovoid contour was observed in the left lateral position (Figure 2). Bronchoscopy revealed a moderate degree of compression of the left main bronchus about two cm. below the carina by an extrinsic mass. The remainder of the examination was normal.

A 22 gauge needle was inserted into the involved area in the fourth interspace in the anterior axillary line and about 300 cc. of crystal clear fluid were aspirated. It was then suspected that the patient had an echinococcus cyst. Examination of the fluid showed scolices of *Echinococcus granulosus* (Figure 3).

The postero-anterior and lateral roentgenograms of the chest taken after the aspiration showed a large cyst with a fluid level. The membranes of the cyst could be seen floating on the fluid (Figure 4). On the same day an increase in temperature occurred. A peak of 102.8° F. was reached in about four days and it returned to normal in about six days.

The roentgenograms of the chest showed an opaque area below the cyst interpreted as pneumonitis. The area of infiltration disappeared in about 10 days under treatment with penicillin and aureomycin.

TABLE III

Authors	Year of Report	Geographical Location	Patients With Involvement of Lungs
Phillips <sup>11</sup>	1934	North America	36
Lilienthal <sup>12</sup>	1934	United States	1
Johns <sup>13</sup>	1934	United States	1
Haight and Alexander <sup>14</sup>	1940	North America	46
Benson, Evans and Zuelger <sup>15</sup>	1943	United States	1
Holman and Pierson <sup>16</sup>	1944	United States	2
Davidson <sup>17</sup>	1944	United States	3
Brewer III, Jones and Dolley <sup>18</sup>	1948	United States	1
Tucker <sup>19</sup>	1951	United States	1
Johnson and Twente <sup>20</sup>	1952	United States	1
Miller <sup>21</sup>	1953	Canada	97
Kergin <sup>22</sup>	1953	Canada	1 (Total unknown)
Harrison <sup>23</sup>	1953	Canada	11
Seley <sup>24</sup>	1953	United States	2

On March 14, thoracotomy on the left side was done through an anterior incision. A portion of the upper lobe was adherent to the thoracic wall. A firm mass about eight cm. in diameter occupied approximately two-thirds of the upper lobe under the adhesions. The mass was grayish-white and easily distinguished from normal pulmonary tissue. Free fluid was not present in the pleural cavity. The area of lung adherent to the thoracic wall was freed by extra-pleural stripping. The apical-posterior and anterior segments including the cyst were resected. A rubber catheter was inserted into the pleural cavity for closed underwater drainage.

The post-operative course was uneventful and the wound healed well. The catheter was removed on the 10th post-operative day. Fluid recovered through the tube was negative for scolices of echinococcus. A roentgenogram of the chest taken on March 28, showed marked clearing of the left lung field. He was discharged from the hospital on March 30 and seen at irregular intervals for examination, the last time being when he was admitted to the medical service of the hospital for a respiratory infection on March 31, 1955. He had no symptom referable to the previous disease. The roentgenogram of the chest was clear (Figure 5). He was discharged from the hospital on April 12.

#### *Comment*

Echinococcus cysts of the lungs are rarely seen in the United States and therefore are frequently forgotten in the differential diagnosis of pulmonary diseases. The difficulty in diagnosis may be considerable and if the laboratory tests are all negative, the diagnosis may not be made until thoracotomy is done. Aspiration for diagnosis preoperatively should not be done because of possible complications.

The various diagnostic tests for hydatid disease should be done in all patients with moderately large or large round lesions of the lung. If these tests are negative, echinococcus disease must be remembered even at the time of thoracotomy. Aspiration of such round lesions should never be done because of the remote possibility that hydatid disease may be present.

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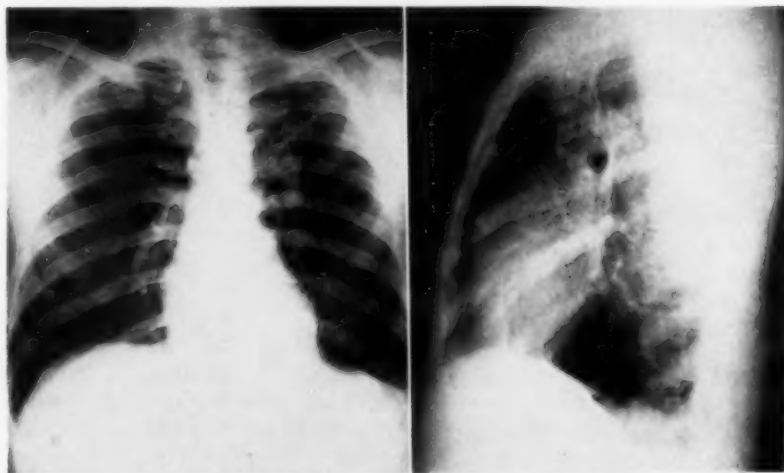


FIGURE 6

FIGURE 7

Figure 6: Postero-anterior roentgenogram of the chest showing clear lungs on April 4, 1955.—Figure 7: Left lateral roentgenogram of the chest showing the lungs to be clear on April 4, 1955.

type of operation varied according to the state of the disease present in the patient and the results were excellent.

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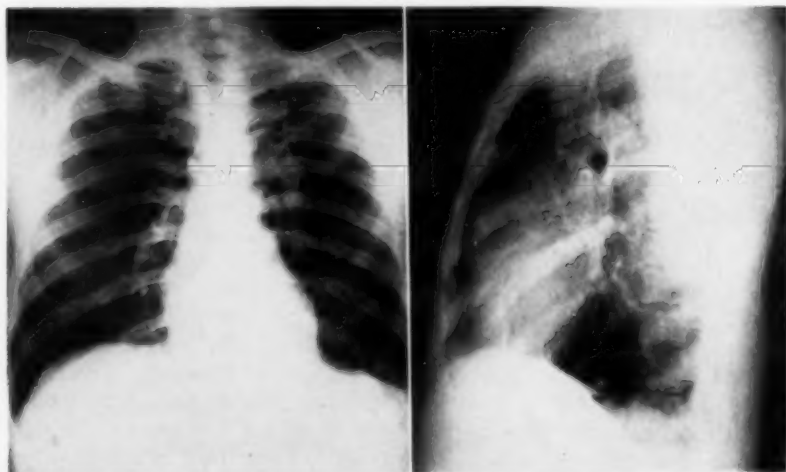


FIGURE 6

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whether the cyst is simple or complicated. In the small simple cysts, enucleation and closure of the resulting cavity by suture should be done. Where the simple cyst is large, segmental resection or lobectomy should be done. A complicated cyst may require segmental resection, lobectomy, pneumonectomy or marsupialization.

#### SUMMARY

Echinococcus cysts of the lung are rarely seen in the United States and therefore are frequently forgotten in the differential diagnosis of diseases of the lung. The incidence of disease due to echinococcus may increase in this country because large numbers of the armed forces have served in areas where infestation is common. The various diagnostic tests for hydatid disease should be done in all patients with moderately large or large round lesions of the lung. If these tests are negative, echinococcus disease must be remembered even at the time of thoracotomy. Aspiration of such round lesions should never be done because of the remote possibility that hydatid disease may be present. The choice of operation in the individual patient must be guided by whether the cyst is simple or complicated. In the small simple cysts, enucleation and closure of the resulting cavity by suture should be done. Where the simple cyst is large, segmental resection or lobectomy is indicated. A complicated cyst may require segmental resection, lobectomy, pneumonectomy, or marsupialization. The diagnosis of an echinococcus cyst was made in a 26 year old Negro who had served in the African and in the Italian campaigns in World War II. Segmental resection was successful.

#### RESUMEN

Como los quistes de equinococo en el pulmón son vistos rara vez en los Estados Unidos, frecuentemente se olvidan en el diagnóstico diferencial de las enfermedades pulmonares.

La incidencia de la enfermedad debida al equinococo puede aumentar en este País debido a que gran número de prsonas de las fuerzas armadas han prestado servicios en las áreas comunmente infestadas.

Las varias pruebas de la hidatidosis deben hacerse en los enfermos todos que presentan lesiones redondas moderadas en tamaño o grandes.

Si estas pruebas son negativas la equinococcia debe recordarse aún durante la toracotomía. La aspiración de tales lesiones nunca debe hacerse ante la remota posibilidad de que se trate de hidatidosis. La decisión operatoria debe depender de que se considere que es una hidatidosis simple o complicada. En los quistes pequeños simples, se puede hacer la enucleación y clausura de la cavidad resultante por sutura. Cuando el quiste es grande se hará resección segmentaria o lobar. Un quiste complicado requerirá ya sea resección segmentaria, lobectomía, neumonectomía o marsupialización. El diagnóstico de la equinococcia se hizo en un negro de 26 años que sirvió en las campañas de Italia y de Africa durante la segunda Guerra Mundial. La resección segmentaria fué realizada satisfactoriamente.

## RESUME

Les kystes hydatiques du poumon sont rares aux Etats-Unis et c'est pourquoi ils sont souvent oubliés dans le diagnostic différentiel des affections pulmonaires. La fréquence de l'échinococcose est susceptible d'augmenter dans ce pays à cause du grand nombre des militaires qui ont servi dans des zones où l'infestation est banale. Les différents tests pour l'affection hydatique devraient être pratiqués chez tous les malades atteints d'opacités arrondies du poumon, qu'elles soient très ou modérément étendues. Même si les tests sont négatifs, l'échinococcose ne doit pas être oubliée au moment de la thoracotomie. L'aspiration de telles lésions arrondies ne doit jamais être pratiquée, à cause de la possibilité d'une maladie hydatique. Le choix de l'opération chez l'individu doit être guidé par le fait que le kyste est simple ou compliqué. Dans les petits kystes simples on devrait pratiquer l'énucléation et la fermeture de la cavité qui en résulte, par une suture. Lorsque le kyste unique est volumineux, une résection segmentaire ou une lobectomie est indiquée. Un kyste compliqué peut demander une résection segmentaire, une lobectomie, une pneumonectomie ou une marsupialisation. Le diagnostic d'un kyste hydatique fut fait chez un noir âgé de 26 ans, qui avait servi lors des campagnes d'Afrique et d'Italie pendant la deuxième guerre mondiale. La résection segmentaire en fut couronnée de succès.

## ZUSAMMENFASSUNG

Echinococcuscysten sieht man selten in den USA und vergisst sie deshalb häufig bei der Differential-Diagnose von Lungenkrankheiten.

Die Häufigkeit einer den Echinococcus zuzuschreibender Krankheit kann in den USA zunehmen, weil beträchtliche Teile der Wehrmacht in Ländern stationiert waren, in denen der Befall alltaglich ist. Die verschiedenen Untersuchungsverfahren auf Hydatiden-Krankheiten sollten bei allen Patienten mit mässig grossen oder mit grossen Rundherden der Lunge vorgenommen werden. Fallen diese Untersuchungen negativ aus, muss man sich an die Echinococcuserkrankung erinnern, selbst zum Zeitpunkt der Thorakotomie. Eine Punktion solcher runder Herde soll man niemals ausführen im Hinblick auf die entfernte Möglichkeit, dass eine Hydatidenkrankheit vorliegt. Die Wahl der Operation im Einzelfall muss davon ausgehen, ob die Cyste einfach oder kompliziert ist. Bei den kleinen einfachen Cysten sollte man eine Enucleation vornehmen nebst Verschluss der sich ergenden Höhle durch eine Naht. In den Fällen, in denen die Cyste gross ist, ist die Segmentresektion oder die Lobektomie angezeigt. Eine komplizierte Cyste kann eine Segmentresektion, Lobektomie, Pneumonektomie oder Cysten-Einnähung erfordern. Die Diagnose einer Echinococcuscyste wurde gestellt bei einem 26 Jahre alten Neger, der in den afrikanischen und in den italienischen Feldzügen im II. Weltkrieg gedient hatte. Es wurde mit Erfolg eine Segmentresektion vorgenommen.

*References will appear in reprint.*



## Pulmonary Ray Fungus Disease Clinical Aspects and Pathogenesis

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Jerusalem, Israel

Pulmonary ray fungus is a relatively rare condition. In 1938 Cope<sup>4</sup> was able to collect 200 cases of pleuro-pulmonary actinomycosis from the literature and Reiter<sup>17</sup> in 1954, noted 47 cases of this disease described during the preceding ten years; of pulmonary nocardiosis only 47 cases have been described.<sup>20-21</sup> It is reported that in large hospitals clinicians encounter three to five cases of pulmonary ray fungus disease over a period of ten years.<sup>4, 10</sup>

In the Rothschild Hadassah University Hospital five cases of thoracic ray fungus diseases were detected during the sixteen year period 1940-1955 and these are described in the present report. Two were cases of actinomycosis and two of nocardiosis; in one case the genus of the ray fungus was not determined.

### Case Reports

#### *Case 1. Actinomycotic pneumonitis of the right upper lobe.*

A 17 year old schoolgirl was admitted to hospital in March, 1954, for an obscure pulmonary condition. The illness began in December, 1953, with pain in both sides of the neck lasting sometimes for a quarter of an hour, sometimes an entire day. These pains, which were aggravated by swallowing and deep inspiration, extended later to the right shoulder and to the right scapular region. In February, 1954, she coughed up a cupful of bright red blood. At the same time her temperature rose to 102.2° F. A radiograph showed a triangular consolidation of the right lung with a small area of translucency at the inferior angle of the opacity (Figure 1).

On admission to hospital she looked well and her temperature was sustained at 37° C. The erythrocyte sedimentation rate (Westergren) was 80 mm. in the first hour and the leukocyte count 8,000 per cm. Sputum culture gave a growth of non-hemolytic staphylococci. Bronchoscopy was without pathological findings and no tubercle bacilli, malignant cells and fungi were detected in bronchial washings. The patient was given penicillin and streptomycin without any observable effect on the clinical or radiological condition. In April, 1954, right thoracotomy was performed (Dr. Milwidsky). The apex of the right lung was found to be infiltrated with hard masses and its separation from the thoracic wall was rendered very difficult by dense adhesions, especially posteriorly and medially. The adhesions involved the brachial plexus, the subclavian artery and the superior vena cava and profuse bleeding occurred during the operation. Biopsy and immediate microscopic examination did not reveal signs of malignancy and resection of the apical segment only was therefore performed. Microscopic examination after fixation revealed chronic inflammation with fibrosis and small abscesses. Within the abscesses colonies of *Actinomyces* were found but it was impossible to identify the species. The patient, after operation, received 76 million of penicillin, 65 gm. of chloramphenicol and 36 gm. of streptomycin over a period of three months and she made a complete recovery.

#### *Case 2. Bilateral actinomycotic bronchopneumonia.*

A 55 year old gardener was admitted to hospital in April, 1955, with the diagnosis of unresolved pneumonia. A week before admission he had developed a severe cough and a temperature of 40.0° C. for which he was treated with penicillin and streptomycin. When admitted to hospital he looked fairly well and was afebrile. Medium-sized rales were heard over the lower parts of both sides of the thorax, especially the left. X-ray film showed a massive homogeneous consolidation in the middle of the left lung field and a smaller net-like opacity of the cardio-diaphragmatic region of the right lung (Figure 2). Erythrocyte sedimentation rate was 75/100 (Westergren)



and leukocyte count 11,000 per cm. Cold agglutinin and ornithosis tests were negative. Sputum examinations were negative for tubercle bacilli and neoplastic cells, but abundant *Candida albicans* were found. In the left submental area a firm, non-painful swelling 4 cm. in diameter was observed. He had noted this swelling one year earlier; it had increased slowly in size, causing slight disturbance of swallowing. His teeth were in poor condition with severe pyorrhea alveolaris. Sputum culture twice gave a growth of anaerobic *Actinomyces israeli*, but more often pure cultures of *Candida albicans* were obtained.

He was treated for four months with penicillin, streptomycin, chloramphenicol, chlortetracycline, oxytetracycline, sulphadiazine and iodides in various combinations. A marked diminution in the size of the submental swelling was observed and radiographs showed a marked improvement in the pulmonary condition. The massive opacity cleared up partially but multiple foci remained in the affected region. The patient, therefore, received two courses of deep x-ray therapy followed again by antimicrobial drugs. However, the infiltrations showed no further improvement. In this case it is possible that a mixed monilio-actinomycotic infection was present.



FIGURE 1



FIGURE 2

Figure 1 (Case 1): Actinomycotic pneumonitis of the apical segment of the right upper lobe.—Figure 2 (Case 2): Bilateral actinomycotic bronchopneumonia.

*Case 3. Lung abscess in descending actinomycosis.*

A 29 year old housewife was admitted to hospital on June, 1941, because of severe pains along the spine accompanied by dyspnoea. Previous history: In May 1939, after the birth of her second child, she developed pain in right haemithorax, temperature 38.5° C, and cough with purulent inoffensive sputum. X-ray film had shown right sided pleural effusion and an opacity with central translucency on right lower lobe (Figure 3). Sputum was constantly negative for tubercle bacilli but in one specimen anaerobic *Actinomyces israeli* was detected. Following three months of sulphonamide therapy disappearance of the opacity and of the effusion was noted. However, in October 1939, an abscess in upper sternal region appeared. This was punctured and pus with abundant sulphur granules was withdrawn. The organism present was diagnosed as anaerobic *Actinomyces israeli*. At this time an exacerbation of a periodontal infection from which the patient had suffered for many years was also noted. A sinus was present in the gum of the left side of the lower jaw and for this she had been treated by the dentist by the application of silver nitrate, three teeth were extracted and the sinus had closed. In 1940 she developed an abscess in left submammary area; this abscess was opened and pus containing *Actinomyces israeli* was again found. A sinus lined with granulation tissue persisted and an oesophagogram performed because of dysphagia showed a free passage of barium from oesophagus to the sinus in the submammary region.

During her hospitalisation in 1941 the sternal and sub-mammary sinuses were treated by radium and deep roentgen-therapy. Moreover, sulphanilamides were given orally and intravenously. Her condition improved, the pains disappeared and the sinuses closed; however, during menstruation reopening of the sinuses and secretion of a small quantity of pus was sometimes observed. During the period 1942-1944 new sinuses appeared at varying intervals, necessitating hospitalisation. The sinuses appeared in the left lumbar region and over the left greater trochanter (November, 1942) left upper gluteal region (March, 1943) and left lower gluteal region (May, 1944). All these sinuses were treated by deep roentgen-therapy and the patient also received sulphanilamides and iodides with good results. A check-up in December, 1945, showed that all the sinuses had closed. Radiographs of chest and spine were without pathological findings.

*Case 4. Haematogenous nocardiosis of the chest and extremities.*

A 46 year old bookseller, in August, 1950, developed superficial painful swellings in the right lumbar region, the right thigh and leg and the left forearm. Later, abscesses

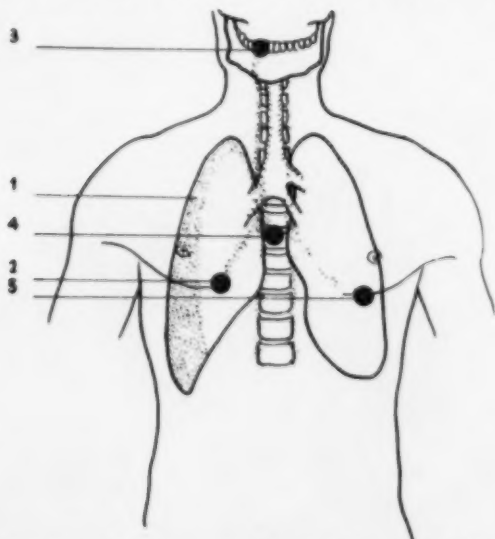


FIGURE 3 (Case 3): Descending actinomycosis. 1. Right pleural effusion (May, 1939). 2. Lung abscess, right (May, 1939). 3. Sinus of the gum of the lower jaw (October, 1939). 4. Sinus in the upper sternal region (October, 1939). 5. Sinus in the left submammary region (March, 1940).

appeared in these regions accompanied by pyrexia. Biopsy and pathological examination showed non-specific inflammation. In September, 1950, x-ray film of the chest showed a large left parahilar opacity. Lateral tomogram showed the opacity to be extrapulmonary and retrosternal, with some pleural thickening and collapse of the lingula. This radiographic finding was not accompanied by any symptoms directly referable to the thorax. When admitted to hospital some days later his general condition was poor and his temperature was 39° C.; erythrocyte sedimentation rate was 104/131 (Westergren) and leukocyte count 22,500 per cm. Blood culture was sterile and no tubercle bacilli were found in the sputum. Biopsy from the abscess of the forearm showed acute purulent inflammation of adipose tissue and a few areas of granulation tissue. In one of these areas a mass of fungus was found which was identified as *Nocardia*.

Treatment, consisting of penicillin, one million units per day and sulphathiazole, 6 gm. per day, was instituted. The temperature subsided and his condition improved. After discharge from hospital the antimicrobial treatment was continued for five months with the addition of chlortetracycline. The abscesses of the extremities healed. A radiograph in 1951 showed almost complete regression of the retrosternal opacity with only pleural thickening still present. He was last seen in 1956 and his condition was excellent.

*Case 5. Nocardial middle lobe pneumonia.*

A 54 year old lawyer was admitted to hospital in December, 1954, with the diagnosis of pneumonia. Two weeks prior to this date he had started feeling tired and had developed a cough with a small amount of yellow, inoffensive sputum tinged with blood. He also gave a history of subtotal gastrectomy for gastric ulcer in 1940 and dental pyrrhoea with abscess formation for some years.

While in hospital his temperature was at first normal but later rose to 39° C.; the erythrocyte sedimentation rate was 92/116 (Westergren) and the leukocyte count 11,600 per cm. X-ray film revealed consolidation of the right middle lobe (Figure 4). Penicillin treatment for two weeks was unsuccessful. Bronchial carcinoma was suspected and bronchoscopy was performed. This revealed redness of the mucosa of the opening of the middle lobe bronchus; mucopurulent secretion was present and this was aspirated. Cytological examination revealed neither neoplastic cells nor tubercle bacilli but some colonies of ray fungus were detected. This organism, seen in smears, grown in cultures, and injected into mice, was identified as *Nocardia*.

He received intensive antibiotic treatment for four months, 103 million units of penicillin, 50 gm. of chloramphenicol, 38 gm. of streptomycin and 120 gm. of sulphadiazine being administered. His chronic gum infection was also treated locally; 12 teeth were extracted and in scrapings from the tooth sockets *Nocardia* was again found. The root of one of the carious teeth was found penetrating the wall of a cyst which was thereafter enucleated. No pathogenic organisms were found in the cyst but it may be



FIGURE 4 (Case 5): Nocardial middle lobe pneumonia. Postero-anterior view.

mentioned that the enucleation was performed after the completion of antimicrobial treatment. He was discharged from Hospital in May 1955, clinically and radiologically recovered.

### Discussion

In discussing pulmonary ray-fungus disease, it is to be stressed that 85 per cent of cases are due to the anaerobic *Actinomyces israeli* and 15 per cent to the acid-fast aerobic *Nocardia asteroides*. Actinomycosis usually spreads by continuity, while in nocardiosis, haematogenous spread is prevalent. In a review of 1,330 cases of actinomycosis, Cope<sup>4</sup> found thoracic localisation in only 15 per cent, while in 62 cases of nocardiosis,<sup>21</sup> the lung was affected in 65 per cent.

The long controversy between Bostroem's<sup>2</sup> "grass chewing" theory which maintained that actinomycosis is due to aerobic organisms which abound in vegetables and gain entrance to the body from the outside, and Israel's<sup>9</sup> "endogenous" theory that the disease is caused by anaerobic organisms which are unable to exist outside the body, has been definitely resolved in favor of the latter theory. The oral cavity is considered the normal habitat of *Actinomyces israeli*; when trauma or infection occurs in the mouth, the organism alters its habits and from being saprophytic becomes parasitic and invades the tissues.

Actinomycotic infection of the mouth is certainly a much more frequent condition than is diagnosed or suspected. Probably many cases diagnosed as simple pyogenic periodontitis are mild infections with the *Actinomyces israeli*. Axhausen<sup>1</sup> was surprised to find sulphur granules in 28 per cent of patients with these mild conditions when tissues excised from the affected area were examined microscopically. There are three routes by which *Actinomyces israeli* can reach the lung from the mouth: 1) via the bronchial tree by aspiration; 2) via the blood stream (septic phlebitis of a small vessel associated with a dental infection); 3) along the fascial planes of the neck and mediastinal structures. In the latter eventuality (Case 3), the spread from the periodontal tissues may have been first to the oesophagus and then by direct spread to the mediastinum structures. The lung involvement could have occurred by way of the bronchi or by direct spread from the mediastinum, which also accounted for the sternal and sub-mammary sinuses. The mediastinal infection may then have descended through one or more of the normal apertures in the diaphragm to the retroperitoneal tissues of the abdomen, thereafter tracking through the posterior abdominal wall in the region of the lumbar triangle of Petit and then to the trochanteric and gluteal areas.

The diagnostic problem of Actinomycosis is complicated by the fact that *Actinomyces israeli* may be found as a saprophyte in the mouths of healthy persons as well as in pulmonary suppurations.<sup>11</sup> Some authors<sup>19</sup> consider these saprophytic ray-fungi to be non-pathogenic *Actinomyces naeslundii*. However, in patients with obscure pulmonary disease compatible with actinomycosis, the demonstration of ray-fungus in the sputum may be considered sufficient proof that the organism is pathogenic.

Antimicrobial drugs have completely altered the clinical course and

progress of ray-fungus disease. In only one of our patients (Case 3) were there multiple sinuses so characteristic of actinomycosis and this case was treated before antibiotic drugs had come into use. In the remaining four cases, the use of antimicrobial drugs from the onset of the disease, even before the diagnosis was made, completely changed the usual course of the disease. Pulmonary actinomycosis, which previously was fatal in more than 50 per cent of cases and nocardiosis with a mortality of 90 per cent are now controllable and curable.

#### SUMMARY

Five cases of pleuro-pulmonary ray-fungus disease are presented—two of actinomycosis, two of nocardiosis and one with genus undetermined. In two the clinicoradiological aspects were those of chronic suppurative pneumonitis. The others had acute and unresolved bronchopneumonia, unresolved middle lobe pneumonia and retrosternal fluid collection with pleural involvement. Three had severe periodontal infection, and in two of them the ray-fungus was detected in the sockets of extracted teeth.

In three cases the lung involvement probably occurred by way of bronchial aspiration and in the remaining cases by direct spread from the mediastinum and by hematogenous spread.

Antimicrobial drugs completely altered the clinical course and prognosis of the ray-fungus disease. In four patients treated with antibiotics from onset of the disease, no sinus was observed and all were cured.

*Acknowledgments:* We should like to thank Professor H. Ungar and Dr. A. Behar of the Department of Pathology, Dr. F. Raubitshek of the Laboratory of Mycology, Dr. H. Milwidsky of the Department of Thoracic Surgery, and Dr. J. Hermel of the Stomatologic Dispensary, whose help was most valuable to us.

#### RESUMEN

Se relatan cinco casos de enfermedad por los hongos radiantes: dos por actinomicosis, dos de nocardiosis y uno de género indeterminado. En dos, el aspecto clínico radiológico era el de neumonitis crónica supurativa. Los otros tenían bronconeumonía aguda no resuelta, neumonía no resuelta del lóbulo medio, y colección retroesternal con compromiso pleural. Tres tenían seria infección periodontal y en dos dellos se encontró el hongo en los alveolos de los dientes extraídos.

En tres casos el compromiso pulmonar ocurrió probablemente por aspiración y en el resto de casos por diseminación directa del mediastino y/o diseminación hematogéna.

Las drogas antimicrobianas alteraron completamente la evolución y el pronóstico de estas enfermedades de hongos radiantes. En cuatro tratados con antibióticos desde el principio de la enfermedad nose observaron fistulas y todos curaron.

#### RESUME

L'auteur présente cinq cas de mycose avec localisation pleuro-pulmonaire: deux cas d'actinomycose, deux de nocardiose et un dû à un germe indéterminé. Dans deux cas, les aspects cliniques étaient ceux d'une pneumonie chronique suppurative. Les autres se présentaient comme une bron-

chopneumonie aiguë, une pneumonie du lobe moyen n'ayant aucune tendance résolutive, et une collection liquidienne rétro-sternale avec atteinte pleurale. Trois malades eurent une sévère infection dentaire, et chez deux d'entre eux le champignon fut découvert dans les alvéoles des dents extraites.

Dans trois cas, l'atteinte pulmonaire survint probablement par aspiration bronchique, et dans les autres cas, par extension directe à partir du médiastin et/ou dissémination hématogène.

Les médications antimicrobiennes ont complètement modifié l'évolution clinique et le pronostic de l'affection mycosique. Les quatre cas traités par les antibiotiques dès le début de l'affection guérissent tous parfaitement.

#### ZUSAMMENFASSUNG

Bericht über 5 Fälle pleuropulmonaler Strahlenpilzerkrankungen: 2 von Aktinomykose, 2 von Nocardiose und 1 unbestätigter Art. Bei 2 Fällen entsprachen die klinisch-röntgenologischen Erscheinungen denjenigen einer chronischen eitrigen Pneumonitis. Die anderen litten an akuter und nicht gelöster Bronchopneumonie, nicht gelöster Mittellappenn Pneumonie und retrosternaler Flüssigkeitsansammlung mit pleuraler Beteiligung. 3 Fälle boten eine schwere periodontale Infektion und bei 2 von ihnen wurde der Strahlenpilz in den Alveolen extrahierter Zähne gefunden.

In 3 Fällen erfolgte die Lungenbeteiligung wahrscheinlich durch bronchiale Aspiration und in den übrigen Fällen durch direkte Aussaat vom Mediastinum oder durch haematogene Aussaat.

Antimikrobielle Medikamente veränderten den klinischen Verlauf und die Prognose der Strahlenpilzerkrankung vollständig. In 4 Fällen, die von Beginn der Behandlung mit Antibiotika behandelt wurden, kam keine Fistel zur Beobachtung und alle wurden geheilt.

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## Treatment of Spontaneous Pneumothorax with Kaolin\*

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Spontaneous pneumothorax, or "pneumothorax simplex," as it has been termed by Kjaergaard, is a relatively common disorder in the apparently healthy young individual. It was first recognized as a clinical entity in 1819 by Laennec, and in 1826 Devellers pointed out the part played by the emphysematous bleb in the development of this condition. Formerly spontaneous pneumothorax was thought to be indicative of pulmonary tuberculosis, but the report of Kjaergaard, in 1932, and subsequent comprehensive reports in the literature have done much to dispel this idea. It is now accepted that spontaneous pneumothorax is due in most instances to the rupture of a subpleural bleb, but in a small majority of cases it may be due to an acquired lesion.

The incidence of a single attack of spontaneous pneumothorax is difficult to estimate from the literature. It has been shown to be relatively common in students and military personnel, and is about four to five times as common in men. Gansler reports an incidence of one per 1,069 admissions at the Sampson Air Force Hospital in the United States. In the Royal Canadian Air Force, over a 10 year period, the incidence is .24 per 1,000, as compared with an incidence of .22 per 1,000 in the Royal Air Force over a six year period. The possibility of a second episode on the same or opposite side is much greater than anticipated. Rumball, in the Royal Air Force, in England, reported a recurrence rate of 24.5 per cent over a five year follow-up, with two cases having four recurrences. Gansler collected 1,080 carefully documented cases from the literature since 1944, and found 142 cases, or 22 per cent had one or more recurrence.

In civilian practice, conservative expectant management of the first attack of pneumothorax simplex is usually carried out, although closed catheter drainage may be required. The lung usually re-expands in three or four weeks, but if re-expansion is slow or prolonged (chronic pneumothorax), or if relapses occur, then detailed investigation and active treatment should be carried out rather than a "laissez faire" approach which is often practised. If spontaneous pneumothorax fails to expand after three months, it should be considered chronic and although it may persist without complications for many years, there is always the danger of the occurrence of emphyema, tension pneumothorax, or bilateral pneumothorax. Shefts, in 114 cases, reported 43 with recurrent or chronic pneumothorax. The chronicity is usually due to adhesions under tension at the base of the torn bleb, or broncho-pleural fistula. Occasionally it may result from pleuritis involving the visceral pleura, which prevents the lung from re-expanding and produces a "captive lung." Bilateral pneu-

\*Presented at the 23rd Annual Meeting, American College of Chest Physicians, New York City, May 29-June 2, 1957.

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mothorax has been reported in 10 to 15 per cent of patients, but in Rumball's group, in the Royal Air Force the incidence was 3 per cent in 142 cases with spontaneous pneumothorax. Haemopneumothorax is an uncommon complication. Jones and Bingham, in 1953, collected 120 cases from the literature, with a mortality of 20 per cent.

In the investigation of pneumothorax simplex, a detailed history is essential. Frequent repeated episodes may be uncovered, although the patient is presented as an initial spontaneous pneumothorax. The family history may be important. Rumball found a history of spontaneous pneumothorax in the parents or siblings in 2 per cent of his cases. In the investigation of all cases a roentgenogram of the chest should be carried out, and this may occasionally reveal large cystic bullous disease, which requires excision. In 142 cases in the Royal Air Force, 10 per cent showed lung bullae on the plain x-ray film, and a further 18 per cent were observed with tomographs. The most certain way of determining the presence of bullae, is by thoracoscopy. A good view of the lung surface is obtained by this method, and the basic pathology is usually determined.

The series to be reported in this paper was started on Royal Canadian Air Force Jet Pilots. It is interesting to note that most of the cases occurred while the flier was on the ground, and only one documented case has occurred in the Royal Canadian Air Force while flying. However, Rumball reports 3 per cent in the Royal Air Force while flying. Amdur has recently reported a case of recurrent episodes of spontaneous pneumothorax due to decrease in barometric pressure, as the result of actual or simulated aerial flight. In this case the only symptom was chest pain, which occurred at altitudes of about 1,200 to 1,500 feet. Roentgenograms were made after altitude chamber flights, and in this

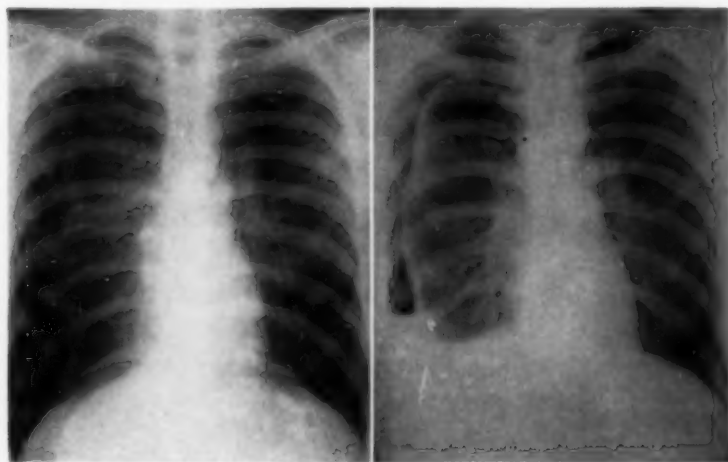


FIGURE 1A

FIGURE 1B

*Figure 1A: Right spontaneous pneumothorax.—Figure 1B: Three days after treatment with Kaolin.*

manner pneumothorax was demonstrated about the apex of the lung, which absorbed quickly at ground level. In the Royal Air Force 56 per cent of the cases of spontaneous pneumothorax occurred at rest, and only 19 per cent during severe exertion. Regulations in the Royal Canadian Air Force prohibit high altitude flying after a single episode of spontaneous pneumothorax, and the low altitude flights require a co-pilot. This is a serious reduction to the Air Force of highly trained flying personnel, as well as a considerable economic loss. According to published reports in Canada, the cost of complete training of a flier to operational activity is approximately \$130,000, and it would appear important, if possible, to rehabilitate this group to flight status. Full flying category has been granted to airmen in the Royal Canadian Air Force following treatment of spontaneous pneumothorax, if complete pleurodesis is obtained. Proof of obliteration of a pleural cavity has been accepted as failure to induce an artificial pneumothorax three months after treatment in at least three sites on the affected side.

This report deals primarily with the production of pleurodesis in the treatment of spontaneous pneumothorax. Experimentally, in 1935, Bethune used pleural poudrage with talc, and produced pleurodesis in patients undergoing lobectomy. Later Singer and Jones, and other investigators used a variety of substances experimentally to produce an aseptic pleuritis. Recently, Ross and Fullerton have drawn attention to the formation of large foreign body reactions in the pleura after the use of talc, which often thickens the pleura to the extent of one centimeter. Gansler stated that the use of talc resulted in talc embolism with hemiplegia in man and experimental animals. Bauer has described the formation of granulomatous masses after the use of talc in abdominal surgery. Thus, it would appear that some patients may be unduly susceptible to contact with talc, and very small quantities may produce a severe reaction. The use of kaolin "Aluminum Salicylate" was first reported by Egger and Good. A single injection of kaolin was used to produce firm pleural adhesions, and later Maxwell recorded a group of 23 cases of spontaneous pneumothorax treated with kaolin suspension, to cause pleurodesis. The minute crystals of kaolin act as an abrasive upon the endothelial lining of the pleura to produce pleuritis. Many other materials, including dextrose solution, human blood, gomenol, silver nitrate, talc, have been used to produce pleural adhesions, but kaolin appears to be effective and efficient, with less morbidity than most of the other chemical substances.

TABLE I

Number of cases	26
Small bulla or bieb	11
Apical scar and/or adhesions	14
No pathology	1

### Procedure

In 26 patients, thoracoscopy was carried out under local anaesthesia in every case, and the pathological processes were noted. Pleurodesis was produced by injecting 3 to 5 cubic centimeters of a 25 per cent suspension of kaolin, or 2 to 3 cubic centimeters of a 50 per cent suspension through the thorascopic cannula, and the air was aspirated from the pleural cavity at the end of the procedure. During the immediate post-operative period, the patient was moved in bed, so that the kaolin could reach all parts of the visceral and parietal pleura. In order to produce complete pleurodesis, a further one or two injections of 2 to 3 cubic centimeters of 25 per cent kaolin solution were given through a needle into the pleural cavity, within seven to 10 days post-operatively. During the post-operative period, a careful observation is made of the pneumothorax space as well as the pleural effusion that results from kaolin injection (Fig. 1B). In a few cases, aspiration of air or fluid may be indicated, but usually this is not necessary. Three months following the completion of the treatment, a test of pleurodesis is undertaken, by attempting to produce pneumothorax in at least three sites on the affected side. A chest roentgenogram is taken to determine the results of the treatment. Maxwell advocated only one injection of kaolin to produce efficient pleurodesis, and there was no recurrence in a follow-up of his cases. Maxwell's procedure would appear satisfactory for civilians, but did not meet the rigid requirements of the Royal Canadian Air Force, who require a test of pleurodesis to ensure that the pneumothorax cannot recur.

### Results

The analysis of the 26 cases treated with kaolin showed that complete pleurodesis was produced on the first attempt in 16 cases, (62 per cent). Eight cases on testing showed partial or loculated pneumothorax and required further treatment. Two of this latter group had a third series of treatments in order to obliterate the pleural space completely. The remaining two did not return for a test of pleurodesis, but according to recent reports, have had no recurrence. Table I indicates the findings on thoracoscopy in this series of 26 patients. A small bulla or bleb was observed in 11 patients, and only in one case was thoracoscopy apparently negative. There was no proved case of pulmonary tuberculosis, but one

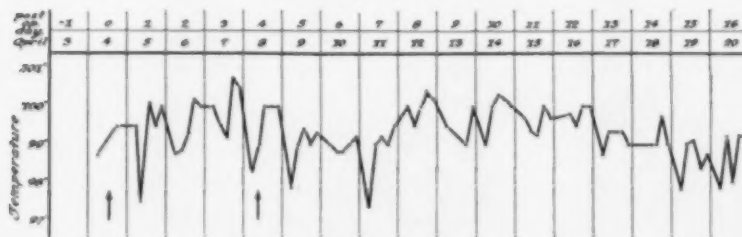


FIGURE 1C

patient with several apical adhesions showed pulmonary shadows on chest roentgenograms, suggestive of arrested pulmonary tuberculosis.

In cases with apical scars, Brock has suggested that spontaneous pneumothorax may be produced by the escape of air from a small emphysematous area, or a minute bulla formed secondary to the scar tissue. Kjaergaard has pointed out the mechanism of production of spontaneous pneumothorax from the rupture of a bleb or bulla, and according to his observations, the cystic area of the lung becomes progressively distended with respiration, and eventually bursts. Occasionally a valvular mechanism may be demonstrated at the base of the bulla, and this was demonstrated in two of Kjaergaard's cases.

There was no serious reaction in the 26 cases when kaolin was used in the accepted dosage. Fluid was aspirated from the pleural cavity in eight patients, and all proved to be sterile on culture. Due to a technical error, there were two cases in which a small amount of kaolin was introduced into the lung parenchyma with a needle. This produced an opaque, round shadow in the lung, which persisted, although in one case the granuloma appeared smaller one year later. Kaolin may be troublesome when used in large quantities. In one patient, not reported in this series, 30 cubic centimeters of 50 per cent kaolin, which is 10 to 15 times the accepted dosage, was injected into the pleural cavity with a needle. This produced rather severe pleuritis, with moderate thickening of the

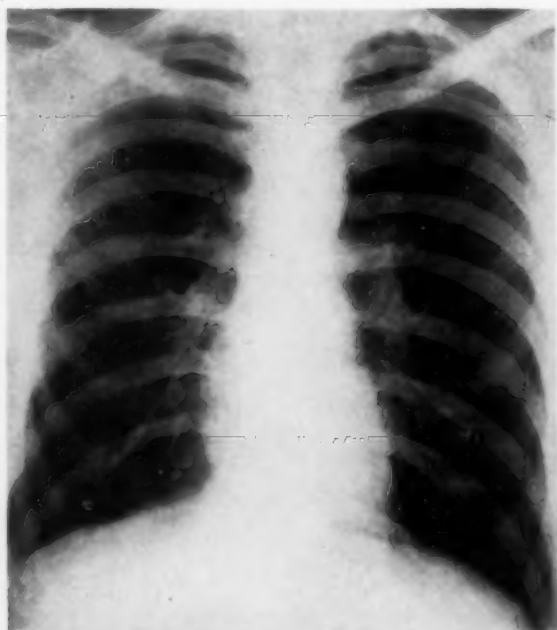


FIGURE 1D: Four weeks after treatment with Kaolin.

visceral pleura, and considerable effusion, which required several aspirations. The lung re expanded over a period of 10 to 12 weeks, and the result was satisfactory, with complete pleurodesis.

### *Discussion*

Although conservative management of the first attack of spontaneous pneumothorax is usually carried out in civilians, active treatment is necessary for flying personnel. Nevertheless, chronic and recurrent cases of spontaneous pneumothorax require careful investigation, including thoracoscopy and treatment. We recommend production of pleural adhesions with kaolin. This is a comparatively minor procedure, and avoids the complications of thoracotomy. If a large cyst or bulla is present, thoracotomy with resection is indicated. Recently Gansler has reported nine cases of spontaneous pneumothorax with extensive subpleural blebs, treated by parietal pleurectomy. In one case haemothorax developed which responded to conservative therapy.

The chief criticism of pleurodesis is the morbidity associated with the chemical pleuritis. In all cases pleural effusion promptly develops, associated with fever and pleuritic pain. Figure 1C illustrates the febrile reaction which develops following the injection of kaolin, as indicated by the arrows on the chart. In this series, it was necessary to obtain a complete pleurodesis, and as a result the morbidity was slightly increased due to repeated injections. It would appear feasible in civilian practice to use only one injection of kaolin, as advocated by Maxwell. In our experience, reaction with kaolin is considerably more satisfactory than many of the other substances previously used.

Pulmonary function studies have not been carried out in this group of patients, but as pointed out by Gansler, there appears to be a distinct difference between the effect of pleural thickening and the occurrence of fibrothorax following chronic emphysema. Paul, Beattie and Blades have reported that open thoracotomy and talcum poudrage for recurrent spontaneous pneumothorax produce no consistent decrease in pulmonary function, as determined by broncho-spirometry in a group of four patients. Clinically in our group, there appeared to be no restriction of movement or pulmonary insufficiency, and of course, there has been no recurrence of spontaneous pneumothorax on the treated side.

### SUMMARY

Treatment of spontaneous pneumothorax by pleurodesis with kaolin suspension has been employed in 26 patients. Obliterative pleuritis appears to reach a maximum at the end of three months, and obliteration of the pleural space was achieved in the first attempt in 62 per cent of the cases. Although there is an appreciable morbidity, this method would appear to be effective and efficient.

### RESUMEN

Se empleó el tratamiento del neumotórax espontáneo mediante la pleurodesis provocada por una suspensión de caolín, en 26 enfermos. La pleuritis



obliterante parece llegar al máximo al cabo de tres meses y la oclusión del espacio se logró al primer intento en 62 por ciento de los casos. No hay apreciable morbilidad y este método parece ser efectivo y eficiente.

#### RESUME

Le traitement du pneumothorax spontané par symphyse pleurale provoquée par une suspension de kaolin a été utilisé chez 26 malades. Une pleurésie oblitérative se constitue et atteint son maximum au bout de trois mois. L'oblitération de l'espace pleural fut obtenue dès la première tentative dans 62% des cas. Bien qu'il y ait un nombre important de manifestations consécutives, cette méthode semble être efficace.

#### ZUSAMMENFASSUNG

Die Behandlung des Spontanpneumothorax mit Pleuraverklebung durch Kaolinaufschwemmung wurde bei 26 Patienten angewandt. Eine obliterierende Pleuritis scheint ihr Maximum zu erreichen am Ende von 3 Monaten, und die Verklebung des Pleuraspaltes wurde in 62% der Fälle mit dem ersten versuch erreicht. Obgleich eine beträchtliche Morbidität besteht, erscheint diese Methode wirksam und listungsfähig.

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## Bronchogenic Carcinoma in Men Under 40 Years of Age

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The world wide experience with bronchogenic carcinoma is one of increasing incidence. It has become the leading cause of death from cancer in men. Clemmesen<sup>2, 3</sup> in a statistical analysis described bronchogenic carcinoma as a "Pandemic" predicting a three- to four-fold increase during the next 30 years.

Along with the increase in occurrence, the disease has been appearing at an earlier age, the peak incidence being younger with each succeeding age group.

At the Fitzsimons Army Hospital 141 male patients have been treated for bronchogenic carcinoma since 1949. Of these 26 (14 per cent) have been below the age of 40. Although a large proportion of patients eligible for care in a military hospital are in the younger age groups, this incidence is similar to the 14 per cent under 40 in Ochsner's<sup>5, 6</sup> collected group of 4,307 cases of lung cancer. Despite the significant incidence of lung cancer in men under 40 it frequently is not considered a significant diagnostic consideration. Furthermore, when the diagnosis is made, an unwarranted hopeless prognosis may be given based solely on the age of the patient.

The following data relates our experience with bronchogenic carcinoma in 26 men under the age of 40.

*Age:* The ages ranged from 20 to 39 with a mean of 33 years. Six of the 26 (23 per cent) were less than 30 years of age.

*Smoking Habits:* Information was available in only 14 cases. There was one non-smoker in this group. His tumor was an adenocarcinoma.

*Symptoms:* The initial symptoms were most commonly cough (41 per cent) representing exacerbation of pre-existing cough or appearance of same. Hemoptysis was uncommon. Chest pain was the complaint initially in 23 per cent of patients. Only two were asymptomatic at the time of diagnosis, the lesion being discovered subsequent to routine chest x-ray film. Other initial symptoms included neck swelling (two) representing cervical metastases and shoulder-arm pain (two) secondary to brachial plexus involvement. The symptom pattern is in accord with that reported by Ariel in an analysis of 1200 unselected cases of bronchogenic carcinoma.

*Bronchoscopy:* Bronchoscopy was performed in 22 (85 per cent). In 13 a positive biopsy was obtained. In two additional cases bronchoscopic

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findings were suggestive of carcinoma but histologic proof was not obtained. Thus a diagnosis was established by bronchoscopy in 50 per cent of the cases (57 per cent of those bronchoscopied). Negative bronchoscopy was noted in only 27 per cent.

*Location and Cell Type:* Fourteen tumors involved the right lung and 12 the left. Eighteen (70 per cent) were located centrally whereas only 30 per cent were related to segmental or smaller bronchi. Nine men (35 per cent) had squamous cell carcinoma. There were eight anaplastic carcinomas (31 per cent), seven adenocarcinomas, and two bronchiolar carcinomas (8 per cent). Except for a higher incidence of adenocarcinoma, these data are in accord with the incidence reported by Neuman<sup>1</sup> for persons at all ages. In those with bronchogenic carcinoma under 40, he reported only 7.8 per cent as having squamous cell carcinoma. Of the six men under 30 one had squamous cell carcinoma, two anaplastic carcinoma and three had adenocarcinoma.

*Treatment:* Sixteen of our cases were inoperable at the time of diagnosis. Inoperability was determined on the basis of distant metastases, cervical node metastases, brachial plexus invasion and extension of the tumor proximal to the carina. There was an average delay of 5.3 months from the onset of symptoms to the establishment of the diagnosis. In most instances the delay was due to failure by the patient to seek early medical attention.

Exploratory thoracotomy was performed in four whose lesions were not resectable. Palliative lobectomy was done in one in the presence of pleural metastases. Segmental resection was performed in another. Four pneumonectomies were done. One of these cases died seven months following resection. A second is living with cerebral metastases, four months after pneumonectomy. One man is living and well 42 months following pneumonectomy for anaplastic adenocarcinoma. Another is well over five years following pneumonectomy and x-ray therapy for squamous cell carcinoma of the left main bronchus. He was 32 years of age at the time of resection. Twenty-one are dead with survival averaging 6.8 months following the establishment of the diagnosis. The longest survival was 29 months in a patient with anaplastic carcinoma. He had no x ray therapy. Treatment with x-ray or nitrogen mustard offered no overall statistical advantage, although it was proved to be of value in individual cases. Those with adenocarcinoma survived an average of 4.3 months compared to the 6.8 months for the squamous cell carcinoma group and 9.5 months for those with anaplastic carcinoma.

#### *Discussion*

Essentially bronchogenic carcinoma is the same disease in young men as in older people. The symptoms, distribution, and cell type are all similar except for moderate increase in the incidence of primary adenocarcinoma.

Thirty-eight per cent of the younger patients were operable when first seen compared to 44 per cent of the entire group of 141 cases. Potentially curative resection was done in 40 per cent of the younger group and 50 per cent of the entire series. Of 30 in the latter group, only two are living over five years with survivors at 44, 21, 18 and 16 months following surgery. Of the four curative resections in the younger age group there are two (three and one-half and five years) long term survivors.

#### SUMMARY

Our experience at the Fitzsimons Army Hospital tends to indicate that bronchogenic carcinoma is no more malignant in those below 40 than in the older age groups. The age of the patient should not mitigate against the diagnosis of bronchogenic carcinoma. The aggressive treatment of young men with bronchogenic carcinoma can yield cures in a number of cases. Two patients in this younger age group of 26, having had definitive extirpative resections, are living and well, three and one-half and five years after surgical management.

#### RESUMEN

Nuestra experiencia en el Hospital Fitzsimonds del Ejército, tiende a señalar que el carcinoma bronquiogénico no es más maligno en los enfermos de menos de 40 años que el de los que pasan de esa edad. La edad del enfermo no debe ser argumento contra el diagnóstico de carcinoma bronquiogénico. El tratamiento agresivo de los hombres jóvenes con carcinoma bronquiogénico puede dar curaciones en cierto número de casos. Dos enfermos entre estos de los más jóvenes tenían 26 años a los que se hicieron extirpaciones definitivas y están vivos y bien después de un año y medio y de cinco años respectivamente, después de la operación.

#### RESUME

L'expérience de l'auteur, à l'Hôpital Militaire Fitzsimons, tend à prouver que le cancer bronchique n'est pas plus malin chez les hommes âgés de moins de 40 ans que chez ceux des groupes plus âgés. L'âge du malade ne devrait pas plaider contre le diagnostic du cancer bronchique. Le traitement énergique de jeunes hommes atteints de cancer bronchique peut apporter des guérisons dans un certain nombre de cas. Deux malades, appartenant au groupe des moins âgés, ayant 26 ans, subirent des exérèses. Ils sont vivants et en bonne santé, trois ans et demi et cinq après le traitement chirurgical.

#### ZUSAMMENFASSUNG

Unsere Erfahrung an Fitzsimons Wehrmachtskrankenhaus geht dahin, anzuzeigen, dass das bronchogene Carzinom nicht stärker bösartig ist bei Personen unter 40 Jahren als in der älteren Altersgruppe. Das Alter des Patienten sollte nicht gegen die Diagnose des bronchogenen Carzinoms ins Treffen geführt werden. Die aktive Behandlung von jungen Männ-

dern mit bronchogenem Carzinom kann in einer Zahl von Fällen Heilungen bringen. 2 Patienten dieser jüngeren Altersgruppe von 26 Jahren, die mit ausgesprochen extirpierenden Resektionen behandelt worden waren, sind am Leben und wohlauf 3½ und 5 Jahre nach der chirurgischen Behandlung.

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# SECTION ON CARDIOVASCULAR DISEASES

## The Value of Left Heart Catheterization in Patients with Rheumatic Mitral Valve Disease

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Diagnostic and therapeutic problems commonly arise in patients with rheumatic heart disease despite the use of all available clinical data, including electrocardiographic and roentgenographic studies. The deficiencies of the conventional aids have become more apparent with attempts to define the physiological significance of mitral valve lesions.

Since its introduction by Cournand and associate<sup>1</sup> in 1941, right heart catheterization has been employed with singular success. Its primary contribution has been in the patient with congenital heart disease, although it has served to clarify much of the altered physiology in patients with rheumatic mitral and tricuspid stenosis. In aortic stenosis and mitral and tricuspid insufficiency, the procedure has been of little value.

In contrast, left heart catheterization enables pressure measurements to be recorded across the aortic valve during systolic ejection and across the mitral valve during ventricular filling.<sup>2, 3</sup>

The present report illustrates the importance of left heart catheterization in the study of patients with rheumatic mitral valve disease. The material is presented in the form of the five most common problems encountered. In each instance, the diagnostic and therapeutic enigma was resolved by left heart catheterization.

All patients were studied by the Fisher<sup>4</sup> modification of the Björk<sup>5</sup> technique.

*Problem 1.* Objective evidence of mitral stenosis combined with equivocal symptoms and a normal roentgenogram and electrocardiogram.

All of the catheterization and other physiological data were supplied by the Brith Sholom Cardiopulmonary Laboratory, Hahnemann Medical College.

This work was supported by the Mary Bailey Foundation for Heart and Great Vessel Research.

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*Case 1:* M. K., a 36 year old white woman, presented a history of lifelong fatigue. Chronic cough was attributed to smoking. Shortness of breath was noted intermittently, but was often sighing in character. Palpitation and precordial aching were mentioned.

Cardiac examination revealed a normal sinus rhythm, a grade 2 apical midiate diastolic rumble with presystolic accentuation, an opening snap and a sharp mitral first sound. The pulmonic second sound was accentuated. Blood pressure was 122/80. The electrocardiogram showed only atrial dysfunction.

The cardiac roentgenograms showed a silhouette that was borderline in size with no clear-cut enlargement of the left atrium (Figure 1).

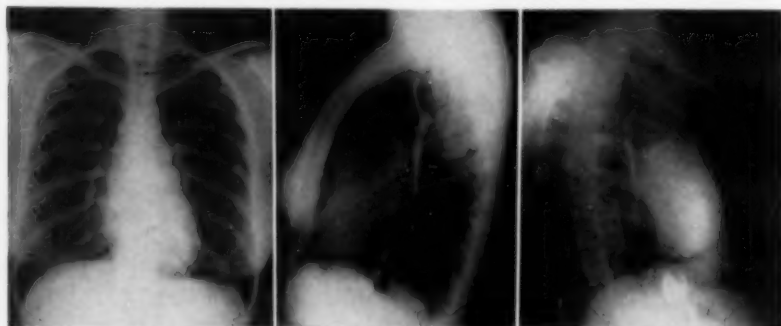
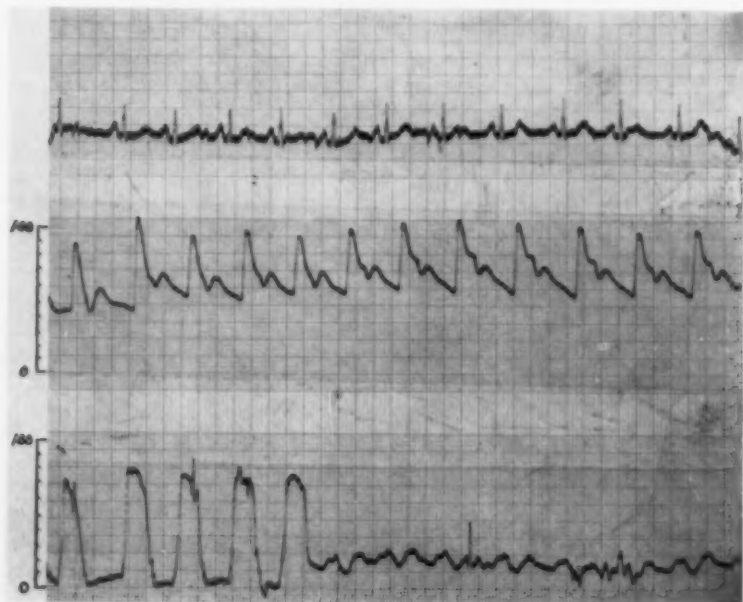


FIGURE 1A

FIGURE 1B

FIGURE 1C

*Figure 1:* P-A, left lateral and right anterior oblique chest roentgenograms of patient M. K. The heart was borderline in size.



*FIGURE 2:* Continuous pressure tracing in patient M. K. as catheter is withdrawn from left ventricle to left atrium. Note ventricular filling gradient. Upper: EKG. Middle tracing is brachial artery pressure curve.

Physiological data are listed in Table I. The mean ventricular filling pressure gradient across the mitral valve was 15 mm. Hg. (Figure 2).

A mitral commissurotomy was performed on July 27, 1955. The mitral valve was finger tip in size and an adequate opening to 1-1/4 fingers was obtained. The tricuspid valve was normal. A follow-up examination several months later revealed that the patient was doing satisfactorily.

*Comment:* Left heart catheterization demonstrated a dynamically significant mitral stenosis when the clinical findings suggested an insignificant narrowing of that valve orifice. Surgery confirmed the presence of a severe mitral stenosis.

*Case 2:* R. G., a 37 year old white woman, presented the chief complaint of fatigue of several years' duration. A slight cough had been present for years. She described four attacks in which she was awakened from sleep by a bad dream with a feeling that she could not catch her breath.

Cardiac examination revealed the presence of a normal sinus rhythm with a characteristic apical midlate diastolic rumble and sharp mitral first sound. The second pulmonic sound was accentuated. The blood pressure was 142/84.

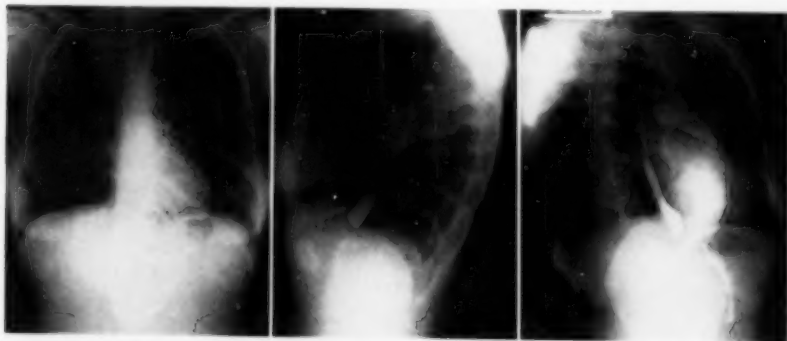


FIGURE 3A

FIGURE 3B

FIGURE 3C

Figure 3: P-A, left lateral, and right anterior oblique chest roentgenogram in patient R. G. Minimal enlargement of the right ventricle, but not the left atrium, was demonstrated.



FIGURE 4: Continuous pressure tracing as catheter is withdrawn from the left ventricle into the left atrium in patient R. G. Note lack of ventricular filling gradient. The unusual contour of the first portion of the atrial curve is related to the position of the catheter directly at the mitral orifice.



The electrocardiogram showed only atrial dysfunction.

The cardiac roentgenograms revealed questionable enlargement of the left atrium only (Figure 3).

The physiological data are listed in Table I. There was no measurable pressure gradient across the mitral valve during ventricular filling even after exercise (Figure 4).

She was advised that she did not need cardiac surgery at the present time.

*Comment:* In contrast to Case 1, this patient, with similar clinical findings, did not have a physiologic obstruction at the mitral valve on left heart catheterization. Hence, conservative management was advocated and it was concluded that this patient's complaints were unrelated to her cardiac lesion. A recommendation was made that the study be repeated in one year to determine the rate of progression, if any, of the rheumatic disease process during this interval.

*Problem 2.* The absence of auscultatory evidence to confirm mitral stenosis when the symptoms, roentgenogram, and electrocardiogram are suggestive of mitral valve obstruction:

*Case 1:* I. K., a 53 year old white woman, had suffered from exertional dyspnea and fatigue for over eight years. There was one bout of pulmonary edema. Intermittent ankle edema was common. A strict cardiac regimen had to be employed.

Cardiac examination revealed a normal sinus rhythm and a grade 3 blowing apical systolic murmur. The mitral first sound was not sharp. The second pulmonic sound was accentuated. There was evidence, on admission, of congestive failure. The neck veins were distended; the liver felt four fingers below the costal margin and 1 plus ankle edema was present. The blood pressure was 125/75.

The electrocardiogram revealed right axis deviation and atrial dysfunction.

The cardiac roentgenograms revealed 3 plus enlargement of the right ventricle and 2 plus enlargement of the left atrium (Figure 5).

The physiological data are presented in Table I. The mean pressure gradient across the mitral valve during ventricular filling was 21 mm. Hg. (Figure 6).

Mitral commissurotomy was performed on November 1, 1955. The mitral valve was heavily calcified with small projections of calcium extending into the valve orifice.

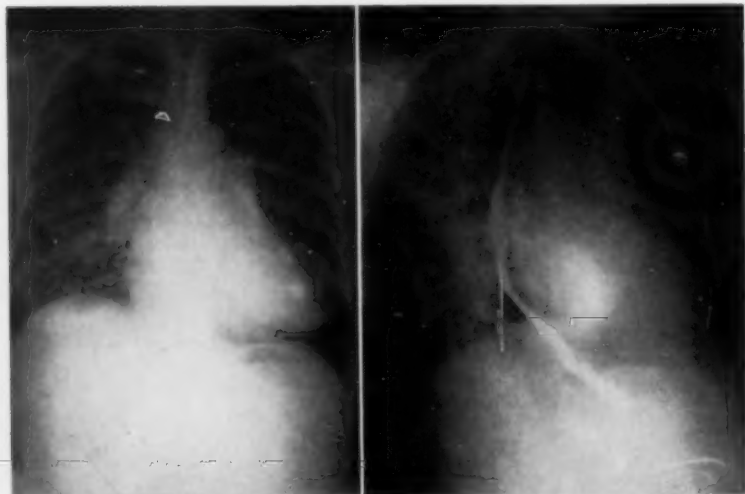


FIGURE 5A

FIGURE 5B

*Figure 5:* P-A and right anterior oblique chest roentgenogram in patient I. K. There was 3 plus enlargement of the right ventricle and 2 plus enlargement of the left atrium.

The opening prior to commissural separation was less than a finger tip and no regurgitation was present. Following surgery, an adequate opening to more than 1 finger was obtained. The tricuspid valve was normal.

*Comment:* The presence of a dynamic obstruction at the mitral valve in patients who lack the typical rough murmur of mitral stenosis has been recorded in our experience in only five cases with normal sinus rhythm. In each, the clinical impression was mitral regurgitation. Only by means of left heart catheterization was the correct diagnosis established and the proper treatment instituted.

*Problem 3.* Clinical manifestations suggestive of co-existing mitral stenosis and insufficiency. The requirement exists to determine which is the major lesion.

*Case 1:* A. Z., a 38 year old white man, presented a clear-cut history of progressive increase in shortness of breath on exertion, fatigue, cough and nocturnal dyspnea. He had been hospitalized three times for acute pulmonary edema. A strict cardiac regimen was employed.

Cardiac examination revealed the presence of atrial fibrillation. A grade 3 blowing systolic murmur combined with a midlate diastolic rumble accompanied by a thrill was present. The pulmonary second sound was markedly accentuated. The blood pressure was 148/88.

The electrocardiogram revealed atrial fibrillation and ST-T changes characteristic of digitalis therapy.

The cardiac roentgenogram demonstrated 3 plus enlargement with involvement of both ventricle and the left atrium (2 plus) (Figure 7).

Physiological data are listed in Table I. Left heart catheterization revealed no pressure gradient across the mitral valve during ventricular filling. A prominent C-V wave was present in the left atrial pressure tracing suggestive of mitral regurgitation (Figure 8). The latter was confirmed at surgery performed for the correction of mitral valve leak.

*Comment:* The patient presented clinical findings consistent with both mitral stenosis and regurgitation. An air of uncertainty was created because of the inability to critically define the relative significance of the

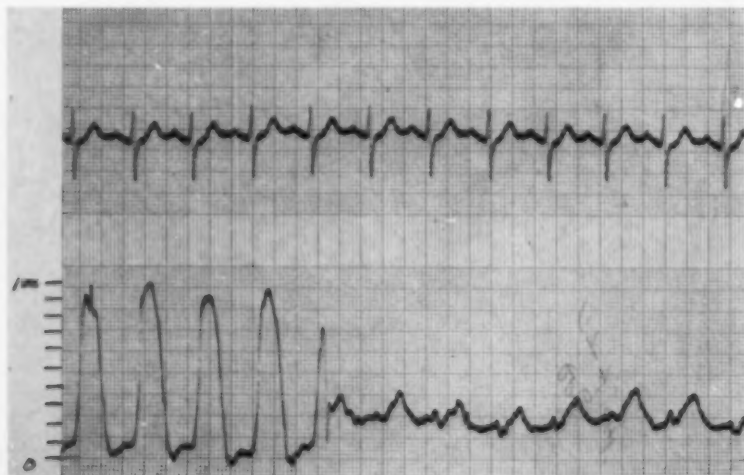


FIGURE 6: Continuous pressure tracing as the catheter is withdrawn from the left ventricle to the left atrium in patient I. K. A marked ventricular filling gradient is demonstrated.

regurgitation and the stenosis. With the left heart catheterization data at hand, the decision to perform surgery for mitral regurgitation was predicated upon the availability of an acceptable procedure for treatment of that lesion and the absence of a gradient across the mitral valve during ventricular filling. The presence of a marked C-V wave in the left atrial curve, though of occasional help in the differential diagnosis of mitral valve lesions, may be seen in patients without dynamic mitral regurgitation, especially in the presence of atrial fibrillation.



FIGURE 7: P-A view of chest in patient in A. Z. Note prominence of hilar vasculature and greater density of the enlarged left atrium.

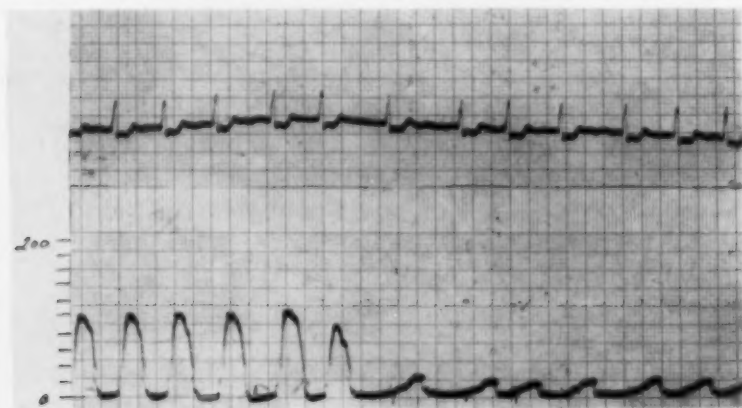


FIGURE 8: Patient A. Z. had mitral regurgitation at surgery. Note lack of ventricular filling gradient and prominence of C-V wave in left atrial curve.

*Case 2:* M. W., a 45 year old white man, presented a history of progressive exertional dyspnea, fatigue, and cough of five years' duration. There had been one severe bout of hemoptysis. More recently, ankle edema had appeared. He was unable to work and required a strict cardiac regimen.

Cardiac examination revealed atrial fibrillation and a grade 3 apical systolic murmur. The mitral first sound was considered sharp. A grade 1 midlate diastolic rumble was heard by some observers. The second pulmonic sound was accentuated. No opening snap was heard. The blood pressure was 130/78.

The electrocardiogram revealed right axis deviation and atrial fibrillation.

The cardiac roentgenograms revealed 3 plus enlargement of the heart with involvement chiefly of the right ventricle and the pulmonary artery segment. There was questionable enlargement of the left atrium (Figure 9).

Physiological data are listed in Table I. Left heart catheterization revealed a ventricular filling pressure gradient across the mitral valve of 25 mm. Hg. (Figure 10).

Mitral commissurotomy was performed on July 20, 1956, and the mitral valve was found to be a tight finger in size. A heavy ridge of calcium was noted at the an-

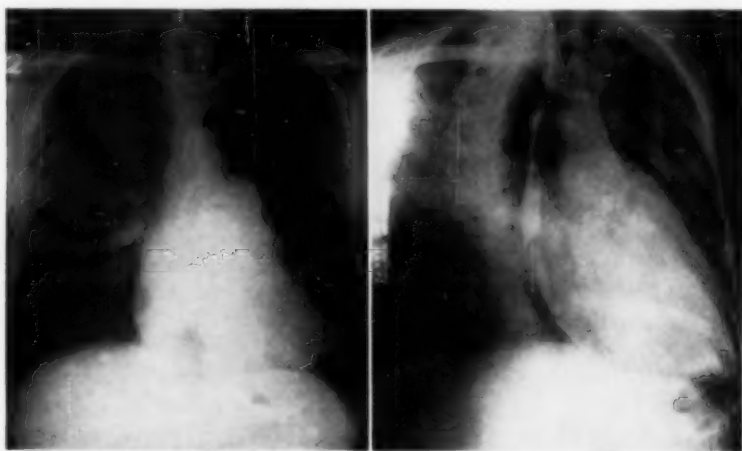
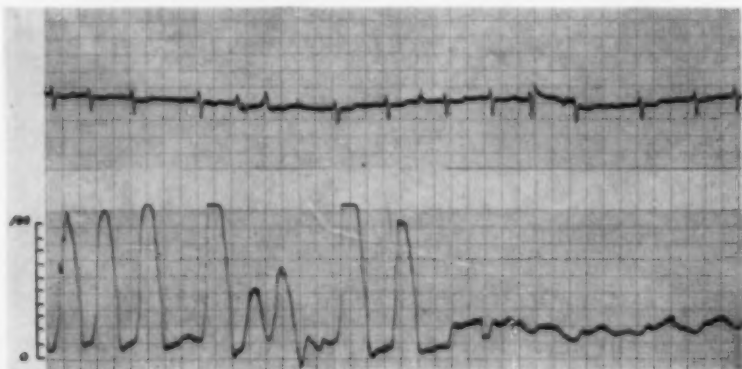


FIGURE 9A

FIGURE 9B

*Figure 9:* Patient M. W. There is marked prominence of the pulmonary artery segment, right ventricle and hilar vasculature. The left atrium is borderline in size.



*FIGURE 10:* Left heart catheterization reveals a marked ventricular filling gradient in patient M. W. Note ventricular extrasystoles. EKG above.

terior commissure. No regurgitation was noted at the mitral valve, and the tricuspid valve was normal. By manual and instrumental techniques, an opening of 2 fingers was obtained.

*Comment:* The intensity of the apical systolic murmur pointed strongly to the diagnosis of major mitral regurgitation. The electrocardiogram and x-ray film did not eliminate this consideration. Left heart catheterization revealed a major stenosis, paving the way to the performance of a successful commissurotomy.

*Case 3:* M. M., a 26 year old white woman, had experienced dyspnea on exertion for two years. Orthopnea was marked and was associated recently with ankle edema and palpitation. A strict cardiac regimen was employed.

Cardiac examination revealed a normal sinus rhythm. The mitral first sound was loud and the second pulmonic sound was accentuated. A faint apical presystolic murmur and a grade 3 blowing systolic murmur, audible over the lower sternum with transmission laterally, were present. The blood pressure was 118/74.

Electrocardiogram indicated right ventricular hypertrophy and strain.

Roentgenogram revealed 3 plus enlargement of the heart with involvement chiefly of the right ventricle. A lesser degree of left atrial and right atrial enlargement was thought to be present.

Left heart catheterization revealed a pressure gradient of 26 mm. Hg. across the mitral valve. The physiological data are listed in Table I.

Surgery was recommended. A tight mitral stenosis with no regurgitation was encountered and an adequate opening was obtained. The tricuspid valve was explored and revealed 3 plus regurgitation.

*Comment:* Clinically, there was wide disagreement regarding the major valve lesion in this case. Some observers argued for mitral stenosis combined with tricuspid regurgitation while others felt that mitral stenosis was present in association with a significant degree of mitral regurgitation. The problem was resolved by left heart catheterization which indicated a tight mitral valve obstruction. A successful commissurotomy was performed and the patient's clinical progress has been excellent.

*Problem 4.* The clinical manifestations unequivocally are those of mitral stenosis. Marked cardiac enlargement initiates the issue as to whether

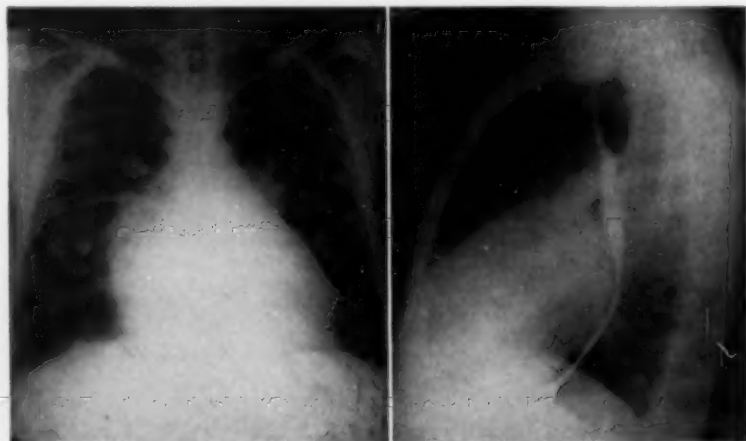


FIGURE 11A

FIGURE 11B

*Figure 11:* Patient A. F. There is marked cardiac enlargement secondary to isolated mitral stenosis.

myocardial degeneration contributes more to the clinical problem than valve obstruction.

*Case 1:* A. F., a 42 year old white man, suffered a cerebral embolism when he was 31 years old. Dyspnea on exertion, chest discomfort, ankle edema, and epigastric discomfort had been present for two years. A second embolic issue occurred in 1956. He was on a strict cardiac program.

Cardiac examination revealed the presence of a normal sinus rhythm with a sharp mitral first sound and a grade 3 midlate diastolic rumble. The pulmonic second sound was considerably accentuated. The blood pressure was 130/80.

Electrocardiogram revealed a normal sinus rhythm with atrial dysfunction.

Roentgenograms revealed a 4 plus enlargement of the cardiac silhouette with in-

TABLE I  
LEFT HEART CATHETERIZATION DATA

Cases	Initial Diagnosis	Rhythm	Pressures		Brachial Artery or Aorta	LA-LV Mean Ventric. Filling Gradient	Final Diagnosis	Operative Findings	
			Left Atrium	Left Ventricle				Valve Orifice Area	Mitral Regurg.
MK	MS of questionable dynamic significance	NSR (20)		80 8	105 55	(68) 15	Dynamic MS	0.70	0
RG	MS of questionable dynamic significance	NSR (4)		116 4	116 78	(90) 0	Dynamic MS		Not Operated
IK	Dynamic MI	NSR (35)		118 9	118 76	(86) 21	Dynamic MS	0.70	0
AZ	Dynamic MS and MI	AF (10)	100 0	130 0	110 70	130 80	0 Dynamic MI	6.0	3+
MW	Dynamic MS and MI	AF (26)	84 5	140 0	84 60	116 82	25 Dynamic MS	0.75	0
MM	Dynamic MS and MI	NSR (26)		112 0	108 72	(82) 24	Dynamic MS Dynamic TI	0.80	0
AF	Dynamic MS	NSR (22)		111 14	136 76	(88) 8	Dynamic MS	0.85	0
LP	Recurrent MS of questionable dynamic signif.	AF (14)	80 10	105 5	85 62	125 70	9 Dynamic MS	1.50	0

All pressures and gradients are expressed in mm. Hg.

Figures in parentheses refer to mean pressures.

The denominator of the fraction under "Left Ventricle" refers to end-diastolic pressure. Mitral valve area is expressed in cm.<sup>2</sup>

volvement chiefly of the right ventricle. The left atrium was enlarged 2 plus (Figure 11).

Physiological data are listed in Table I. A gradient across the mitral valve of 8 mm. Hg. was found.

Cardiac surgery was performed on March 4, 1956. The mitral valve was a finger tip in size with some subvalvular fusion and valvular calcification. An adequate opening was obtained. The tricuspid valve was normal.

*Comment:* Clinically, everything pointed to the presence of pure mitral stenosis. Yet, a gradient of only 8 mm. Hg. was detected across the mitral valve. This was attributed to a poor cardiac output resulting from associated myocardial disease. The anticipated result from mitral commissurotomy in such cases may be less than ideal.

*Problem 5.* The diagnosis of restenosis of the mitral valve.

*Case 1:* L. P., a 39 year old woman had a mitral commissurotomy performed in May of 1955 because of dyspnea, fatigue, edema, hemoptysis and recurrent attacks of pulmonary edema. The preoperative diagnosis of mitral stenosis was confirmed at operation and an adequate opening was obtained to one and three-fourths fingers without the production of mitral regurgitation.

She remained in asymptomatic state until a short while before her readmission to Hahnemann Hospital on March 25, 1956. Her symptomatic pattern was exactly similar to that described prior to her original operation one year previously.

Cardiac examination revealed atrial fibrillation, a sharp mitral first sound, an opening snap, and an accentuated pulmonic second sound. A presystolic accentuation of a loud midlate apical diastolic rumble, and a grade 2 apical systolic blow were noted.

The electrocardiogram showed atrial fibrillation and right ventricular hypertrophy.

The roentgenograms revealed 2 plus enlargement of the right ventricle and left atrium. There was no alteration in size and configuration since the date of original mitral valve surgery.

The physiological data are listed in Table I. Left heart catheterization, performed on March 28, 1956, revealed a ventricular filling gradient across the mitral valve of 9 mm. Hg.

She was re-operated and a tight mitral stenosis again was encountered. A successful commissurotomy was performed for the second time.

*Comment:* The recurrence of cardiac symptoms in a patient who has been operated previously for mitral stenosis poses many problems. One must evaluate the adequacy of the medical regimen and the contribution to the clinical picture of other valve lesions, not correctible at the time of the original mitral commissurotomy. The myocardial factor must be appraised. None of these appeared to play a significant role in the above case. Rather, left heart catheterization confirmed the presence of a significant gradient across the mitral valve. Surgery was decided upon and a tight mitral stenosis without regurgitation was actually encountered and relieved.

### Discussion

With the introduction of left heart catheterization, a method has been provided which clarifies the dynamics at the mitral valve itself. Usually, there is no measurable difference in pressure between the left atrium and the left ventricle during ventricular diastole. The constant physiological abnormality in mitral stenosis is the presence of a pressure gradient during ventricular filling. When this information is combined with an estimation of the cardiac output, the degree of mitral stenosis can be precisely determined and the valve orifice area calculated. This is best accomplished by combined heart catheterization.<sup>5</sup> The complications and hazards of this procedure are generally minimal.<sup>6</sup>



It is natural to accept left heart catheterization for the study of those cases in whom the clinical aids have failed to accurately assay the physiological significance of rheumatic mitral stenosis. The measurements obtained at left heart catheterization also have been of value when marked discrepancies exist between the symptomatic picture and the classical signs of the disease. The objectivity provided by the determination of pressure gradients also permits the application of more exact criteria in the selection of cases for cardiac surgery. This information helps to eliminate the confusion that constantly arises in the borderline case concerning the type of future management.

Finally, left heart catheterization offers an acceptable method for evaluating the results of surgery.<sup>7</sup>

The indications for left heart catheterization in rheumatic heart disease will probably increase. Its use is envisioned in the routine study of the inexorable progression of the rheumatic process at the mitral and aortic commissures.

#### SUMMARY AND CONCLUSIONS

1. The value of left heart catheterization in patients with rheumatic mitral valve disease is documented.
2. Case histories are presented in which therapeutic and diagnostic problems were resolved by the attainment of the ventricular filling gradient across the mitral valve.
3. Left heart catheterization is chiefly of value in patients with rheumatic heart disease in whom marked discrepancies exist between the objective and subjective clinical picture.
4. Left heart catheterization also is helpful in evaluating the results of cardiac surgery and analyzing the progression of the rheumatic process following mitral commissurotomy.

#### RESUMEN Y CONCLUSIONES

1. El valor de la cateterización cardiaca izquierda en enfermos con enfermedad valvular reumática de la mitral, se justifica.
2. Se presentan dos historias en los que los planes de diagnóstico y de tratamiento se resolvieron alcanzando el gradiente de llenado ventricular a través de la mitral.
3. La cateterización cardiaca izquierda es principalmente de valor en los enfermos con enfermedad cardiaca reumática en los que existen discrepancias marcadas entre los cuadros clínicos subjetivo y objetivo.
4. La cateterización cardiaca izquierda también es útil para valuar los resultados de la cirugía cardiaca y para analizar la evolución del proceso reumático después de la comisurotomía mitral.

#### RESUME

1. Les auteurs apportent des documents militant en faveur du cathétérisme du coeur gauche chez les malades atteints de maladie mitrale.
2. Les auteurs présentent des observations où la thérapeutique et le

diagnostic sont liés au remplissage progressif du ventricule à travers la valvule mitrale.

3. Le cathétérisme du coeur gauche est de grande valeur chez les malades atteints de rhumatisme articulaire aigu, chez lesquels existent des divergences marquées entre les signes cliniques objectifs et subjectifs.

4. Le cathétérisme du coeur gauche est également utile pour évaluer les résultats de la chirurgie cardiaque et analyser l'évolution du processus rhumatismal à la suite de la commissurotomie mitrale.

#### ZUSAMMENFASSUNG UND SCHLUSSFOLGERUNGEN

1. Die Bedeutung der Katheterisierung des linken Herzens bei Kranken mit rheumatischer Erkrankung der Mitralklappen wird unter Beweis gestellt.

2. Es werden Krankengeschichten gebracht, deren therapeutische und diagnostische Programme zur Lösung kamen durch die Kenntnis des ventrikulären Füllungs-Druckgefälles durch die Mitralklappen hindurch.

3. Die Katheterisierung des linken Herzens ist von besonderem Wert bei Kranken mit rheumatischer Herzerkrankung, bei denen ausgeprägte Diskrepanzen bestehen zwischen dem objektiven und dem subjektiven klinischen Bild.

4. Die Katheterisierung des linken Herzens ist ausserdem eine Hilfe bei der Auswertung der Ergebnisse der Herzchirurgie und Analyse des Fortschreitens des rheumatischen Prozesses im Anschluss an eine Mitralkommissurotomie.

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# The Frequency of Tricuspid Stenosis with Particular Reference to Cardiac Surgery

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## *Introduction*

The diagnosis of tricuspid stenosis is often overlooked clinically. In the past, emphasis on correct diagnosis has often been stressed only as a clinical triumph of physical diagnostic methods or from the prognostic aspect. Cardiac catheterization studies have increased the possibility of establishing the presence of tricuspid stenosis, thereby overcoming the inherent limitation in making this diagnosis on clinical grounds alone. Recent successes with tricuspid commissurotomy<sup>1, 2, 3</sup> offer additional incentive to clinicians to identify these patients. It would therefore be of interest to know the potential number of individuals with tricuspid stenosis who could benefit from commissurotomy.

The literature includes few reports of such data. Isolated or collected case reports offer no help in this regard. In most reported series of cases of rheumatic heart disease, little or no distinction is made between tricuspid stenosis, tricuspid insufficiency, and incidental tricuspid disease without significant changes in cardiac dynamics.

Cooke and White<sup>4</sup> reviewed 4,300 autopsies from the Massachusetts General Hospital from 1920 to 1937 and found 217 cases of rheumatic heart disease with involvement of the tricuspid valve in 47. Their report is based on five cases with marked stenosis and 25 with slight to moderate tricuspid stenosis. Smith and Levine<sup>5</sup> studied 4,437 autopsies performed at the Peter Bent Brigham Hospital during the years 1913 to 1940. They found 340 cases of rheumatic valvular disease. Among these, there were 11 with marked, and 10 with slight tricuspid stenosis. All had an accompanying mitral stenosis and in 75 per cent aortic stenosis was also present. Garvin<sup>6</sup> selected 119 who died primarily of rheumatic heart disease among 6,548 autopsies at the Cleveland City Hospital from 1930 to 1939. Thirteen (10.9 per cent) had definite tricuspid stenosis but the degree of this stenosis and the presence of a concomitant stenosis of the mitral and/or the aortic valve is not stated. None of the reports reviewed indicated the frequency of severe tricuspid stenosis in a series with severe mitral and/or aortic stenosis. Therefore, it was decided to analyze a consecutive series of patients examined post-mortem and uniformly evaluated and classified by one observer.

## *Materials and Methods*

A series of 8,676 consecutive necropsies performed at the Queens General Hospital from 1936 to 1950, inclusive, was reviewed. Five hundred

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and nine (5.9 per cent) of these were classified as rheumatic heart disease by fulfilling the following criteria: (1) fusion and retraction of the mitral or tricuspid valves; (2) fusion and shortening of the chordae tendinae; (3) noncalcific fusion of the aortic valve; (4) any fusion, including calcific changes, of the aortic valve when it was associated with definite rheumatic mitral and/or tricuspid valve involvement; (5) active rheumatic heart disease with Aschoff bodies or characteristic verrucae; (6) bacterial endocarditis of the mitral or aortic valves with some evident previous distortion, but the exact estimation of the severity of rheumatic damage being difficult. Cases showing the following changes were excluded from the rheumatic category: (1) slight mitral or tricuspid valve changes (for example, tongue-like extensions of the valve cusps), or distortion which did not fulfill the criteria state above (points 1 and 2); (2) slight aortic stenosis with or without slight mitral or tricuspid involvement; (3) calcific aortic stenosis with or without slight mitral or tricuspid valve changes; (4) calcification of the valve rings alone. Thus, 103 cases of calcific aortic stenosis and 72 cases of doubtful origin were excluded from this study."

The severity of the rheumatic valvular stenosis was graded from 1 to 4 plus, with 1 plus being the least severe involvement, yet sufficient to meet the criteria above, and 4 plus being the most severe involvement and represented by valves described as "fish-mouth," "button-hole," "slit-like," "markedly stenotic," "could not admit one finger"; 2 and 3 plus represented the intermediate degrees of severity.

In the present study, 82 cases with bacterial endocarditis were excluded. In addition, those in the first two decades of life were not included because they usually showed evidence of rheumatic activity, and because patients in this age group are usually not accepted for cardiac surgery of this type.

### *Results*

There were 282 residual cases with severe (3 to 4 plus) rheumatic mitral or aortic stenosis, or both. Of these, the mitral valve alone was severely involved in 168 (59 per cent); the aortic valve alone in 33 (12 per cent); both valves were severely affected in 81 (29 per cent).

An additional 17 (5.7 per cent) had severe or moderately severe tricuspid stenosis. Nine of these were associated with mitral stenosis as the only other severe valvular lesion; eight occurred in hearts with severe involvement of both the mitral and aortic valve. Isolated rheumatic tricuspid stenosis was not encountered.

It should be noted that the present cases were selected only on the basis of severe morphological valvular stenosis without regard for most of the clinical criteria used in the selection of patients for commissurotomy.

### *Comment*

These findings indicate that an additional 5.7 per cent of patients with severe stenosis of the mitral and/or aortic valves may be benefited by commissurotomy for an associated tricuspid lesion. This additional increment may be considerably increased if many of the patients with severe

mitral and/or aortic stenosis alone are eliminated on the basis of the usual clinical criteria for selecting cases for such commissurotomy.

It has been noted that patients with tricuspid stenosis survive for a longer time after the onset of heart failure compared to other rheumatic valvular diseases.<sup>4</sup> This observation concerning longevity with failure offers an additional incentive to discover such bedridden patients who may have been classified as ineligible for commissurotomy. In some of these cases surgical intervention may be withheld because of inadequate evaluation of the role of the tricuspid lesion in producing this status. Some patients who are now disqualified from surgery for mitral stenosis may well have an undiagnosed concomitant tricuspid stenosis. It is possible that such individuals could benefit from adequate surgical treatment because the "protective" role of the tricuspid stenosis on the mitral stenosis allows longer survival after the onset of heart failure.<sup>4</sup> Consideration might well be given to enlarging the clinical criteria for commissurotomy in such cases.

In occasional cases with recurrence of symptoms after temporary relief due to mitral commissurotomy the explanation may be found in the unmasking of a tricuspid lesion. Subsequent tricuspid commissurotomy substantially improved such a patient.<sup>2</sup> Similarly, the clinical response to mitral commissurotomy has been further improved by a tricuspid commissurotomy performed later.<sup>7</sup> Yu et al.<sup>8</sup> have also noted that "in a patient with combined mitral and tricuspid stenosis, the expected improvement may not occur unless both mitral and tricuspid valves are fractured."

Previous studies have indicated the potentially greater opportunity for embolization when cases with combined severe aortic and mitral stenosis were compared to cases with severe stenosis of only the mitral valve.<sup>9</sup> The most important of these complications is cerebral embolization. Additional tricuspid commissurotomy per se, would not significantly increase this occurrence since embolic material from the right side of the heart does not have access to the systemic circulation.

All of these considerations make it worthwhile to establish the diagnosis of existing tricuspid stenosis. This requires a renewed awareness of the historical, physical diagnostic, electrocardiographic, and radiologic features of this lesion and a continuing suspicion of its existence in appropriate circumstances with the use of newer diagnostic techniques such as cardiac catheterization when indicated.

#### SUMMARY AND CONCLUSIONS

In a series of 509 consecutive autopsied cases of rheumatic heart disease, there were 282 instances of severe stenosis of the mitral and/or aortic valves. An additional 17 (5.7 per cent) had an associated tricuspid stenosis which might be benefited by commissurotomy.

Because this series is based on morphologic alterations without regard for the clinical criteria for the selection of patients for cardiac surgery, it is suggested that this group may be larger than is apparent from this

figure. The unmasking of unrecognized tricuspid stenosis following mitral commissurotomy and improvement after subsequent tricuspid commissurotomy is noted.

The diagnosis of tricuspid stenosis is no longer only a question of prognosis and of academic interest as an exercise in clinical diagnosis. Increased awareness of the frequency of tricuspid stenosis, careful clinical observation of patients with rheumatic heart disease, and the use of newer techniques such as cardiac catheterization to detect this lesion may permit surgical benefit for such patients.

#### RESUMEN

En una serie de 509 casos autopsiados de enfermedad reumática cardíaca, hubo 282 casos de estenosis acentuada de la mitral o de las válvulas aórticas. Además hubo 17 (5.7 por ciento) de estenosis tricuspídea acentuada que podrían beneficiarse por la comisurotomía.

Como esta serie se basa en los cambios morfológicos sin tener en cuenta el criterio clínico para la selección de los casos para cirugía cardíaca, se sugiere que este grupo puede ser mayor de lo que aparentan estos números. El descubrimiento de la estenosis tricuspídea no conocida después de comisurotomía mitral y la mejoría después de comisurotomía tricuspídea se hace notar.

El diagnóstico de la estenosis tricuspídea nos da solamente un asunto de pronóstico y de interés académico como ejercicio de diagnóstico clínico. El aumento del estado de alerta ante la frecuencia de la estenosis tricuspídea, la cuidadosa observación clínica de los enfermos con enfermedad reumática y el uso de nuevas técnicas tales como la cateterización cardíaca para descubrir esta lesión pueden permitir un beneficio quirúrgico para estos enfermos.

#### RESUME

Dans une série de 509 autopsies pour rhumatisme articulaire aigu, il y eut 282 cas de sténose grave des valvules mitrale et/ou aortique. Il faut y ajouter 17 cas (5,7%) dans lesquels s'associe une sténose grave de la tricuspide, qui auraient pu bénéficier d'une commissurotomie.

Cette série a été choisie en fonction des alterations morphologiques, sans s'occuper des critères cliniques pour décider de l'intervention chirurgicale. Il apparait dès lors que ce groupe pourrait être plus étendu qu'il ne semble d'après ce tableau. Les auteurs notent l'absence de symptômes de sténose de la tricuspide et son ignorance après commissurotomie mitrale, alors que l'amélioration survint après commissurotomie de la tricuspide.

Le diagnostic de sténose de la tricuspide n'est pas seulement une question de pronostic et d'intérêt théorique, pas plus qu'un exercice de diagnostic clinique. Une connaissance accrue de la fréquence de la sténose de la tricuspide, une observation clinique soigneuse des malades atteints de rhumatisme articulaire aigu, et l'emploi de techniques plus nouvelles, telles que le cathétérisme cardiaque pour découvrir cette lésion peuvent permettre le traitement chirurgical de tels malades.



## ZUSAMMENFASSUNG

In einer Reihe von 509 aufeinander folgend sezierten Fällen von rheumatischer Herzerkrankung ergaben sich 282 Beispiele von schwerer Stenose der Mitralklappen und/oder der Aortenklappen. Weitere 17 (5,7%) hatten damit verbunden eine schwere Tricuspidal-Stenose, die von einer Commissurotomie Nutzen gezogen hätten.

Weil diese Reihe basiert auf morphologischen Veränderungen ohne Bezug auf die klinischen Kriterien zur Auswahl von Patienten für die Herzchirurgie, wird angenommen, dass diese Gruppe grösser sein könnte als es nach diesen Zahlen den Anschein hat. Es wird die Entlarvung unerkannter Tricuspidal-Stenosen im Anschluss an eine Commissurothomie der Mitralklappen festgestellt und ihre Besserung nach anschliessender Commissurothomie der Tricuspidalklappe.

Die Diagnose der Tricuspidal-Stenose ist nicht länger nur eine Frage der Prognose und von akademischem Interesse als Übungsgegenstand für klinische Diagnosen. Vermehrtes Gewährwerden der Häufigkeit von Tricuspidal-Stenosen, sorgfältige klinische Beobachtung von Patienten mit rheumatischen Herzerkrankungen und der Gebrauch von neueren Techniken, wie etwa Herzkatheterisierung zur Feststellung dieses Befundes können einen Gewinn für solche Patienten auf chirurgischem Wege bedeuten.

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# Postoperative Coronary Thrombosis and Myocardial Infarction

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Surgical intervention in persons with degenerative heart disease constitutes a growing proportion of all surgical procedures. While the total population of the United States has been increasing gradually, the recent numerical increase in the elderly has been rapid and great. In 1940, the percentage of population over 55 years was 14.8 per cent; it is estimated in 1980 it will approach 27.2 per cent.<sup>1</sup> The often repeated statement that a compensated heart is capable of withstanding surgery as well as a normal heart has fostered an erroneous feeling of security not justified in arteriosclerotic heart disease. Referring to patients with valvular, hypertensive and non cyanotic heart disease, Levine<sup>2</sup> recognized a close correlation between cardiac functional capacity and ability to withstand surgery. However, referring to those with arteriosclerotic heart disease, he stated "the risk of surgery is possible two or three times greater than it is with those of the same age where hearts are normal." A review of the literature (Table I) shows the incidence of postoperative myocardial infarction in patients with history of coronary insufficiency to be 1.0 to 7.1 per cent.

## *Method of Study*

A review of postoperative myocardial infarctions and coronary thromboses was made at the Coral Gables Veterans Administration Hospital covering the period March 1, 1949 through March 1, 1956. An evaluation of the patient's preoperative cardiovascular status and operative and postoperative courses were undertaken in an effort to better anticipate and prevent future operative cardiovascular complications.

Cases of myocardial infarction were included only when an unequivocal diagnosis was established either by serial electrocardiograms or by necropsy findings. Cases in which the diagnosis was made clinically without such confirmation were deleted from the study. Since pathological changes in hearts of the aged are frequent, special attention was directed toward examination of gross and microscopic material in order not to misinterpret age of the pathological process. Because of likely differences in pathogenesis, material was carefully studied to establish either a thrombotic or non-thrombotic etiology of the infarction. The definition of the postoperative period was that used by Carp<sup>3</sup> and included the period through the 30th day after operation.

## *Results*

During the period of this study, 20 patients were found to have developed postoperative coronary thromboses or myocardial infarctions. The average

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age was 62, with a range of 48 to 78. All were white men. Although the total number of operations performed during the period of this study is not known, 400 patients with preoperatively recognized arteriosclerotic heart disease underwent surgery. Eight of the 20 who sustained the postoperative complications were considered free of coronary heart disease at the time of surgery; 12 were recognized preoperatively to have arteriosclerotic heart disease. Therefore, the incidence of postoperative myocardial infarction or coronary thrombosis in the group with recognized coronary artery disease was 3 per cent. Five of the 12 patients with arteriosclerotic heart disease had a preoperative history of angina pectoris; 10 of the 12 had previous myocardial infarction. Four of the latter 10 had remote infarction demonstrated by preoperative electrocardiographic study while the history for infarction was allegedly negative.

On the basis of the highest repeated preoperative blood pressure, two patients were hypertensive. Their blood pressures were minimally increased according to the criteria of White. One had associated heart disease of another etiology.

#### *Type of Operation and Anesthesia*

Seven operations were classified as elective and 13 as urgent (Table IV). In the urgent group, operative intervention was deemed necessary to preserve life. Elective operations were those in which the underlying condition was not otherwise rapidly or necessarily fatal, or for which adequate non-surgical measures were available. Since complications were not confined to major surgery, the study was based on both major and minor surgical procedures. Simple biopsy or drainage of a readily accessible structure was not included. Diagnostic and therapeutic paracenteses were not included, nor were spinal taps or proctoscopy in the absence of associated surgical procedures. When more than one operation was performed in a single patient, each procedure was considered separately. Eight operations were performed under spinal anesthesia. Four had procedures done under local anesthesia, and the remaining eight had general anesthesia, cyclopropane being the primary anesthetic agent in each of the eight cases (Table IV).

#### *Laboratory Studies*

Eight of the 20 (40 per cent) patients had either at the time of surgery, or at the predicted time of myocardial infarction, significant anemia (Table II). The range of anemia was 7.5 gm., to 11.5 gm., per 100 cc., with a mean of 9.9 gm. per 100 cc. Four of the anemias were secondary to acute blood loss and four were of a chronic type secondary to infection, toxemia, or metastatic malignancy.

#### *Operative Shock*

Seven patients developed shock during surgery with systolic drops of 50 mm. Hg., or greater, and diastolic drops in excess of 25 mm. Hg. (Table III). One episode of shock was for five minutes, and the remainder for 20 minutes or more, with a maximum duration of 60 minutes. Two

additional patients showed lesser drops in blood pressure, one from 120/68 to 90/52 mm. Hg. for a five-minute period, and the other from 110/50 to 85/40 mm. Hg. for a 30-minute period. Two of the patients developing operative shock had anemia due to acute blood loss. Of the seven, four had general anesthesia, and three spinal. Four of the 20 failed to have pulse rates recorded during the operative procedure because surgery was done under local anesthesia. Of the 16 who had records of operative pulse rates, six (37.5 per cent) developed tachycardia which was of a rate and duration considered, relative to preoperative status, significantly abnormal. All six demonstrated rates between 110 to 140 per minute.

#### *Postoperative Myocardial Infarction and Coronary Occlusion*

Postoperative myocardial infarction was demonstrated by electrocardiogram in 10 of the 20 patients. In the remaining 10, postoperative electrocardiograms were not taken either because of the lack of suspicion of the occurrence of the cardiac insult, or demise was sudden and did not permit time for such confirmation. By dying on the day of surgery, two patients, who had no electrocardiograms taken, had the time of their infarction established within a 24 hour period. An additional three developed typical symptoms and died before an electrocardiogram could be obtained. Altogether, the day of infarction was established in 15 of the 20, and ranged from the day of surgery to the 23rd postoperative day. Although all 20 had the cardiac complication within one month of surgery, the exact time could not be established in five patients. Forty-seven per cent had their infarction during the first three postoperative days. This percentage compares with a three-day incidence of 51.5 per cent in Master's<sup>4</sup> series of postoperative myocardial infarctions and 60 per cent in Wroblewski's<sup>5</sup> Memorial series.

The obtunding of the sensorium and alteration of pain threshold by postoperative medication appeared to disguise the more common manifes-

TABLE I  
INCIDENCE OF POSTOPERATIVE MYOCARDIAL INFARCTION

	PREOPERATIVE			POSTOPERATIVE	
	Coronary Insufficiency	Angina Pectoris	Myocardial Infarction	Myocardial Infarction Number	Deaths
Brumm & Willius <sup>3</sup>	257		32	8 (3.1%)	8
Hannigan et al. <sup>7</sup>			58	4 (7.1%)	1
Morrison <sup>13</sup>			37	2 (5.4%)	1
		58		2 (3.4%)	2
Etsten & Proger <sup>6</sup>	517			5 (1.0%)	5

tation of coronary insufficiency. Only six of the 20 patients had pain as a symptom of the infarction or occlusion. The remaining 14, while free of pain, had various combinations of the following pain equivalents: weakness, malaise, cold sweats, apprehension, and syncope. The atypical cardiac picture occurring in the postoperative period is frequently confused with other operative complications, including pulmonary emboli, pneumonia, infection, hemorrhage, and abdominal crises. Congestive failure was a frequent associated finding and was noted in five patients. Although shock was commonly observed, it was difficult to determine whether it was a cause or a manifestation of the myocardial infarction.

The large percentage of deaths in this small series (75 per cent) reflects the utilization of postmortem records in compiling case material. Fourteen patients underwent necropsy examination. Of these, six (43 per cent) were found to have both a fresh coronary thrombosis and a recent myocardial infarction. Seven (50 per cent) had a fresh myocardial infarction in the absence of a demonstrable occlusion, and one (7 per cent) had just a recent coronary thrombosis with no other evident cause of death. Of the seven who developed operative shock, four came to postmortem study, and three were found to have non-thrombotic myocardial infarctions. The incidence of non-thrombotic myocardial infarctions in this small group was greater than that appearing in series of postmortem studies of non-postoperative myocardial infarctions. In Blumgart's<sup>6</sup> series, only 12 of 45 (27 per cent) hearts with non-postoperative acute myocardial infarction showed neither acute coronary thrombosis nor acute coronary occlusion.

TABLE II  
HEMOGLOBIN AT TIME OF INFARCTION OR OCCLUSION

Patient	gm. hb. per 100 cc.
J.C.	7.5
W.M.* +	10.5
J.M.* +	11.0
G.S.*	10.5
L.K.* +	8.5
L.S.	11.0
H.R.	11.5
R.G.* +	9.0
	mean 9.9 gm. per 100 cc.

\* developed operative shock

+ due to acute blood loss

Of the 14 patients in this study who came to autopsy, eight died solely as a result of cardiac complication. Six were found to have complicating processes which, in addition, were probably etiologically related to death. The associated findings included extensive metastases, septicemia and acute suppurative pyelonephritis, cerebrovascular accidents, focal hemorrhages in brain and adrenal, and peritonitis.

### Report of Cases

Summaries of five cases are presented to demonstrate a probable association between the preoperative cardiovascular status, the operative course, and the subsequent postoperative cardiac complication.

*Case 1:* L. K., a 61 year old man, with a negative history of coronary insufficiency, had cystoscopy performed for evaluation of hematuria of recent onset. An electrocardiogram taken prior to the procedure showed "non-specific T-wave changes." At the time of induction of spinal anesthesia, the hemoglobin was 8.5 gm. per 100 cc. The blood pressure promptly dropped from 130/68 to 75/40 mm. Hg., and hypotension and a clinical picture of shock persisted for a 45-minute period. The immediate postoperative course was uncomplicated. On the 16th day myocardial infarction occurred.

*Comment:* Prolonged shock occurred following induction of spinal anesthesia in a patient with a marked anemia secondary to acute blood loss. With preoperative blood replacement, the occurrence of shock and subsequent appearance of infarction might have been avoided.

*Case 2:* J. M., a 51 year old man, with a remote history of myocardial infarction and recent angina pectoris, had an excision of a "stitch abscess" of the anterior abdominal wall. The procedure was done under local anesthesia. On the third postoperative day, symptoms of coronary insufficiency were noted to be increasing and an acute myocardial infarction was recognized. At the estimated time of the infarction the hemoglobin had dropped from a preoperative level of 14.0 gm. to 10.5 gm. per 100 cc. After several days of additional observation, a large growing hematoma of the anterior abdominal wall was noted and was recognized to be responsible for the drop in hemoglobin.

TABLE III  
OPERATIVE SHOCK  
(Occurred in 7 of 20 patients)

Pt.	Pre-op. B.P. in m.m. Hg.	Maximum drop in m.m. Hg.	Duration of hypotension	Range of operative pulse per minute
W.M.	150/100	80/75	20 minutes	110-110*
H.T.	150/90	80/?	5 minutes	120-142
G.S.	140/80	88/44	60 minutes	110-120
L.K.	130/68	75/40	45 minutes	120-130
J.R.	140/90	0/0	20 minutes	90-108*
J.M.	130/60	80/?	60 minutes	95-110
R.G.	168/88	75/60	15 minutes	90-110*

\* Rate unchanged over preoperative rates.

*Comment:* Acute blood loss in the immediate postoperative period resulted in diminution of an already decreased coronary blood flow. Prompt recognition of and replacement of the blood loss may have helped prevent coronary insufficiency and avoided the myocardial infarction.

*Case 3:* W. M., a 61 year old man, with a history of angina pectoris and a remote myocardial infarction, had surgical intervention for a bleeding peptic ulcer. Hemoglobin at the time of surgery was 10.5 gm. per 100 cc. A subtotal gastric resection was done under general anesthesia. The preoperative blood pressure was 150/100 mm. Hg. Coincident with traction on the stomach, drops in blood pressure occurred with a low of 82/75 mm. Hg. Hypotension persisted for a 20-minute period. Death occurred on the fourth postoperative day due to an acute coronary thrombosis and myocardial infarction.

*Comment:* A patient with recognized coronary artery disease had anemia, due to acute blood loss, at the time of surgery. The operative hypotension was the likely cause of the postoperative infarction. The anemia and the hypotensive autonomic reflex were probably etiologically related to the shock.

*Case 4:* H. T., a 55 year old diabetic man, had a negative history of coronary insufficiency. An emergency appendectomy was performed without taking a preoperative electrocardiogram. The blood pressure at onset of surgery was 150/90 mm. Hg. Following induction of spinal anesthesia, blood pressure dropped to 80/0 mm. Hg. In spite of prompt and continuous use of L-arterenol through time of death on the second postoperative day, the blood pressure frequently dropped below 100/65 mm. Hg. Postoperatively, an electrocardiogram was taken and it demonstrated both a recent and remote myocardial infarction.

*Comment:* Because of a negative history for coronary insufficiency, a preoperative electrocardiogram was not obtained. Had this been avail-

TABLE IV  
DATA ON THE 20 PATIENTS

Pt.	Recognized ASHD	Operation	Anesthesia	Duration in minutes
W.T.	O	Herniorrhaphy - E	spinal	85
J.C.	*	Embolectomy and amputation (3 stages) - U	spinal	45,60,85
W.M.	o	Subtotal gastrectomy for hemorrhage - U	general	135
J.M.	*	Excision of mass of abdominal wall - E	local	95
A.H.	*	Cholecystectomy for acute cholecystitis - U	general	105
H.T.	*	Appendectomy - U	spinal	105
G.S.	O	Exploratory for cancer of pancreas - U	general	180
T.W.	*	Herniorrhaphy - E	spinal	105
M.B.	*	Cystoscopy for calculus - U	local	7
M.M.	o	Gastrectomy for cancer - U	general	150
L.K.	O	Cystoscopy for hemorrhage - U	spinal	105
L.S.	O	Cystoscopy for obstruction - U	local	7
E.W.	*	Cholecystectomy for chronic cholecystitis - E	general	165
J.R.	*	Sympathectomy for gangrene of leg - U	general	135
H.R.	O	Skin graft to leg - E	spinal	7
J.M.	O	Closure of perforated ulcer - U	general	135
G.H.	O	Orchidectomy for cancer of prostate - E	general	60
G.F.	O	Excision of cancer and skin graft - U	local	15
R.G.	*	Abdominal-perineal resection - U	spinal	180
F.M.	*	Hydrocelectomy and orchidectomy - E	spinal	60

E - Elective surgery      U - Urgent surgery



able, the remote infarction would have probably been demonstrated. With the knowledge of the existing coronary artery disease, the potentially hypotensive producing spinal anesthesia would have been avoided, and the necessity of a more aggressive treatment of hypotension would have been apparent.

*Case 5:* M. B., a 55 year old diabetic man, with a previous history of myocardial infarction, was cystoscoped under topical anesthesia for evaluation of symptoms of renal colic. The immediate postoperative condition was satisfactory but was soon followed by a septicemia and acute myocardial infarction. Death occurred on the eighth postoperative day. In addition to the finding of myocardial infarction and pseudomonas septicemia, a suppurative pyelonephritis was found.

*Comment:* The non-cardiac postoperative complications of the surgical procedure probably further impaired the coronary reserve by increasing cardiac work and decreasing coronary blood flow.

### Discussion

Recent emphasis in the study of postoperative coronary thrombosis and myocardial infarction has been largely directed towards a disturbance of the clotting tendency during the postoperative period. Although the general consensus of most authors is that a state of hypercoagulability of the blood is a frequent postoperative finding, there has been considerable disagreement regarding the etiology of the altered clotting tendency, and the time of the estimated peak of the increased clotting. In spite of the many studies of altered clotting tendency in the postoperative period, little of value has resulted regarding prevention of coronary thrombosis and myocardial infarctions. That other, or additional, factors productive of such postoperative disasters exist and better lend themselves toward prophylaxis is likely. Masters *et al.*,<sup>7</sup> discussing acute coronary insufficiency, enumerated three factors precipitating that state: sudden increase in cardiac work, diminution of coronary blood flow, and interference with oxygenation of blood. A study of the postoperative myocardial infarctions and coronary occlusions at the Coral Gables Veterans Administration Hospital demonstrates the frequent association of a protracted state of coronary insufficiency and the occurrence of subsequent cardiac complications.

Apprehension associated with impending surgery, and excitement with anesthetic induction increase blood pressure and heart rate and thereby increase cardiac work. Release of epinephrine produces tachycardia and serves as a trigger mechanism for the development of inefficient arrhythmias. The likelihood of the occurrence of the latter is enhanced by anoxia and hypercapnia incident to excessively deep anesthesia.

Diminution of coronary blood flow from drops in blood pressure and decrease in cardiac output must be avoided lest one developed operative and postoperative cardiac complications. The causes of operative shock include blood loss, peripheral vasodilatation secondary to deep anesthesia, and reflex vasodilatation due to autonomic reflexes. Opdyke<sup>8</sup> showed that in hemorrhagic shock coronary flow is decreased by 30 to 66 per cent. Masters<sup>9</sup> studied 103 cases of moderate and severe hemorrhage in which one or more electrocardiograms were obtained during the stage of active



bleeding. Fifty-nine presented signs of acute coronary insufficiency. That operative intervention in the absence of shock is not void of changes on the heart was demonstrated by Kurtz.<sup>10</sup> He described electrocardiographic abnormalities in 80 per cent of a series of 109 patients under anesthesia. Mendelsohn and Monheit<sup>11</sup> noted during surgery electrocardiographic changes in 70 per cent of a group of cardiac patients and in 30 per cent of a group of non-cardiac patients. It has been shown that abdominal cardiac reflexes are more likely to develop in previously damaged hearts. Mendelsohn and Monheit<sup>12</sup> took operative electrocardiograms and noted electrocardiographic changes during surgical manipulation in 50 per cent of 30 cardiac patients. With spinal anesthesia, a blocking of vasopressor impulses causes a drop in peripheral resistance, and a pooling of blood on the venous side of the circulation occurs. An awareness of the potential danger of spinal anesthesia in the poor risk patient will decrease the frequency of cardiac complications.

Interference with oxygenation of blood during the operative period as a result of inadequate airways, and hypoventilation due to obtunding of the respiratory center by medication, or over-estimation of the excursions of the rebreathing bag, set the stage for grave cardiovascular complications. Restricting bandages and pain are responsible for shallow breathing. Extremes of position on the operating table are known to compromise the chest as an organ of respiration, to impair the circulation by causing pooling of blood, and to produce the dangerous Valsalva maneuver, the latter interfering with the role respiration plays in propelling blood into the thorax.

The presence of anemia interferes with optimal oxygenation of tissues. As stressed by Beling,<sup>13</sup> "replacement of blood is not only safe for patients with cardiac disease, it is mandatory." The importance of determining preoperative blood volumes is well recognized. That a decrease in blood volume plays as important a role as does anemia in the development of coronary insufficiency secondary to shock has been demonstrated by the equally corrective effect of infusions of plasma and blood on the electrocardiographic changes of insufficiency. By means of radioisotopes, easier and more accurate methods of determining blood volumes are now available and should be utilized preoperatively in both debilitated patients and in those who recently suffered from acute blood loss.

Complicating pathological processes tend to further impair the coronary reserve by increasing cardiac work and by decreasing coronary blood flow. A marginal coronary blood flow, sufficient to carry a patient through an operative procedure without complications, may prove inadequate in the face of associated non-cardiac complications.

That the postoperative complications of coronary occlusion and myocardial infarction are not to be found limited to the field of geriatric surgery, is attested to by the growing frequency of the finding of degenerative heart disease in the young and middle-aged. In order to better prevent postoperative coronary occlusions and myocardial infarctions, we cannot take for granted the general health of any patient undergoing surgery.

The most important tool available in recognizing an underlying coronary insufficiency is the cardiac history. Such a history will be of greater importance than the cardiac findings on physical examination. The responsible physician should be well-grounded in the basic principles of eliciting a good cardiac history, and the care with which he takes a cardiac history should be as detailed as that directed towards an evaluation of the underlying surgical condition. An electrocardiogram will serve as an invaluable supplement to the history, and will provide evidence of remote myocardial infarctions and recent coronary insufficiency.

The finding of arteriosclerotic heart disease in a patient suffering from a surgically remediable illness need not result in the patient being denied the opportunity of having the trouble corrected. When confronted with urgent surgical intervention, a recognition of associated arteriosclerotic heart disease will permit a coordinated effort of the surgeon, anesthesiologist, and internist, directed towards prevention of, and prompt correction of, coronary insufficiency in the preoperative, operative, and postoperative periods. A recognition of coronary artery disease prior to elective surgery will alert one to the knowledge that such a procedure cannot be undertaken with impunity.

#### SUMMARY

The frequency of postoperative myocardial infarction or coronary thrombosis at the Coral Gables Veterans Administration Hospital in patients with recognized arteriosclerotic heart disease was 3 per cent. A review of the operative and postoperative courses of these patients demonstrates a frequent association of protracted states of coronary insufficiency and the occurrences of subsequent cardiac insults. Anemias at the time of surgery, operative tachycardia and shock, and noncardiac complications were productive of coronary insufficiency by interference with oxygenation of blood, decreasing coronary blood flow and increasing cardiac work.

The most important tool available in recognizing an underlying coronary insufficiency is a detailed cardiac history. An electrocardiogram serves as an invaluable supplement by providing evidence of remote myocardial infarction and recent coronary insufficiency. Recognition of arteriosclerotic heart disease will necessitate a coordinated effort directed towards prevention, and prompt correction, of coronary insufficiency in the preoperative, operative and postoperative periods.

#### RESUMEN

La frecuencia del infarto cardiaco postoperatorio o de la trombosis coronaria en el Hospital de los Veteranos de Coral Gables fué de 3 por ciento. Una revisión de la evolución operatoria y postoperatoria de estos enfermos demuestra una asociación frecuente de estados prolongados de insuficiencia coronaria y el acaecimiento de subsecuentes daños cardiacos. La anemia durante la cirugía, la taquicardia operatoria y el shock y complicaciones no cardiacas producen insuficiencia coronaria por la inter-

ferencia con la oxigenación de la sangre, el decrecimiento del flujo de las coronarias y aumento del trabajo cardíaco.

El instrumento de mayor importancia para reconocer la insuficiencia coronaria subyacente es una historia cardíaca detallada. Un electrocardiograma sirve como un invaluable agregado para proporcionar evidencia de infarto cardíaco remoto o una reciente insuficiencia de coronarias. El reconocimiento del corazón arterioescleroso necesitará un esfuerzo coordinado hacia la prevención y la pronta corrección de la insuficiencia de coronarias en las etapas pre, trans y postoperatoria.

#### RESUME

La fréquence de l'infarctus myocardique ou de la thrombose coronarienne post-opératoires fut de 3% chez les malades atteints d'athérome à l'Hôpital de l'Administration des Vétérans de Coral Gables. Une étude de l'évolution opératoire et post-opératoire de ces malades démontre l'association fréquente d'une insuffisance coronarienne latente et de manifestations cardiaques ultérieures. Les anémies survenant au cours de l'intervention, les tachycardies et le choc opératoires, les complications non-cardiaques furent génératrices d'insuffisance coronarienne, par l'intermédiaire des troubles de l'oxygénation sanguine, de la diminution du débit du sang coronarien et de l'augmentation du travail cardiaque.

Le moyen le plus important pour identifier une insuffisance coronarienne latente est l'histoire cardiaque détaillée. L'électrocardiogramme est d'un secours inestimable pour apporter la preuve d'un infarctus myocardique ancien et d'une insuffisance coronarienne récente. La reconnaissance d'une affection cardiaque athéromateuse nécessitera la coordination des efforts en vue de la prévention et de la rapide de l'insuffisance coronarienne dans les périodes pré-opératoire, opératoire, et post-opératoire.

#### ZUSAMMENFASSUNG

Die Häufigkeit des postoperativen Myocardinfarktes oder der Coronar-thrombose lag im Coral Gables Kriegsversehrten-Fürsorgekrankenhaus bei Patienten mit nachgewiesener arteriosclerotischer Herzerkrankung bei 3%. Eine Durchsicht des operativen und postoperativen Verlaufes dieser Kranken ergab eine häufige Verknüpfung eines protrahierten Zustandes von Coronar-Insuffizienz mit dem Auftreten darauffolgender cardialer Insulte. Anaemie zur Zeit der Operation, Tachycardie und Schock während des Eingriffes und Nicht-cardiale Komplikationen förderten die Coronar-Insuffizienz durch Störung der arterialisierung des Blutes, Herabsetzung der coronaren Blutdurchströmung und vermehrte Herzleistung.

Das wichtigste Instrument, das zur Erkennung einer bestehenden Coronar-Insuffizienz zur Verfügung steht, ist eine ins Einzelne gehende cardiale Vorgeschichte. Ein EKG dient als eine unschätzbare Stütze bei der Gewinnung von Anhaltspunkten für einen verborgenen Myocardinfarkt und eine frische Coronar-Insuffizienz. Die Feststellung einer arteriosclerotischen Herzerkrankung wird eine gleichgeschaltete Bemüh-

ung notwendig machen hinsichtlich Verhütung und prompter Korrektur der Coronar-Insuffizienz während der praeoperativen, operativen und postoperativen Zeitabschnitte.

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## CURRENT THERAPY

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### The Selection of an Antibiotic for the Treatment of Bacterial Endocarditis

Prior to the advent of potent bacteriostatic and bacteriocidal agents, it was common practice to subdivide cases of bacterial endocarditis into two groups: *acute bacterial endocarditis*, i.e. bacterial endocarditis of less than the three or four weeks' duration, and *subacute bacterial endocarditis*, which persisted for more than four weeks. The discovery and utilization of present-day antibiotics have changed the entire picture and course of bacterial invasion of the endocardium and made the distinction meaningless. Preferably, in classification emphasis should be placed on the specific organism responsible for the bacterial invasion and, where known, the name of the organism should be made a part of the disease designation.

Some bacteria prove relatively resistant to penicillin; others actually produce a specific penicillin-destroying enzyme known as penicillinase. Bacteria which are resistant to penicillin are in some cases susceptible to large doses of the antibiotic. Bacteria which are penicillin-resistant but with individual cells sensitive to the action of the antibiotic form an important group: their sensitivity, as measured in the laboratory, may vary 1,000-fold or more according to the inoculum. Whether or not such organisms will be affected by large doses of penicillin would, therefore, seem to depend more on heaviness of infection than on resistance of the organism as determined by laboratory tests.

Although the organism most commonly responsible for bacterial endocarditis in patients with rheumatic valvular disease or congenital lesions of the heart and vessels is *Str. viridans*, this organism poses little problem in therapy because—along with pneumococci, gonococci and group A hemolytic streptococci—strains of *Str. viridans* all are moderately or highly susceptible to penicillin therapy. Enterococci, which are relatively resistant to penicillin alone, now account for about 15 per cent of cases, contrasted with 4 or 5 per cent in the pre-antibiotic era. Endocarditis due to enterococci or coliform organisms occurs most frequently in patients with infections of the genitourinary or the intestinal tract or after various diagnostic or therapeutic procedures carried out in these areas.

Most stubborn, chronic cases of bacterial endocarditis today are caused by staphylococci. Infection with staphylococci produces hypersensitivity toward these organisms: although the patient builds up a fair degree of immunity toward further overwhelming invasions of micrococci, paradoxically he responds with definite lesions to amounts of exotoxin so minute they would pass unnoticed in ordinary persons. Staphylococci have been

found at the site of venous cut-downs, may follow the insertion of catheters for continuous venous infusions, or may gain entrance with the needle of the narcotic addict. Apparently more resistant or more serious cases of staphylococcal endocarditis now are met in our hospitals, and fully 80 per cent of these patients die, as compared with only 66 per cent in former years. Our present impotence in the face of staphylococcal endocarditis may be attributed to three factors: (1) failure to identify the organism and to recognize its virulence; (2) inadequacy of treatment; and (3) delay in instituting treatment. With these factors in mind, we see that the most effective program is the immediate institution of treatment—even before the organism is identified. At the same time, blood culture should be undertaken to determine, if possible, the specific organism responsible. Once the organism has been identified and its sensitivity to various antibiotics determined, antibiotic attack can be directed against that specific organism. Large doses of multiple antibiotics should be used, with sufficient amounts of antibiotic given to cause blood levels between three and four times those indicated in the sensitivity studies. In cases where blood cultures remain negative despite persistence of the clinical picture of endocarditis, the patient should be treated heroically, i.e., with very large doses—40 to 60 million units of penicillin, 1 to 2 grams of streptomycin, and 1 to 4 grams of chloromycetin daily, dosage dependent upon the severity of the invasion and virulence of the organism.

A note of caution: whenever possible, narrow-spectrum antibiotics should be used rather than the broad-spectrum preparations, which disturb normal body flora and thus encourage the superimposition of micrococcic organisms.

In a number of instances, congestive failure will set in or increase as a result of the healing process after the endocarditis has been eradicated, and deaths in these patients often are due to this complication. Awareness of this possibility and prompt management of the failure are necessary, especially at the time that the patient again becomes ambulatory.

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## THE ELECTROCARDIOGRAM OF THE MONTH

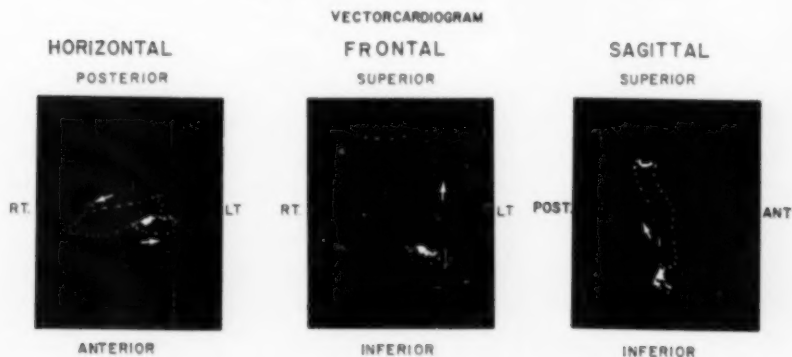
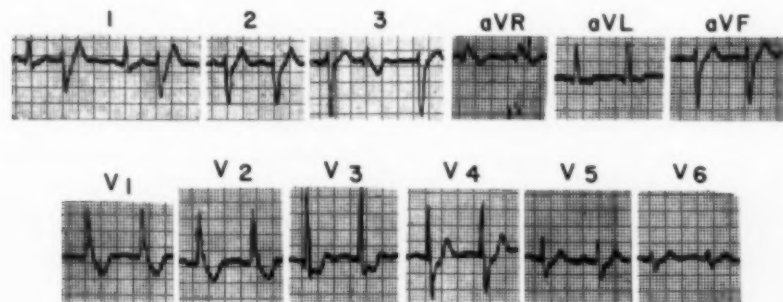
*The author would be pleased to receive comment and controversy from readers in relation to explanations offered*

M. S. is a 56-year-old white man who was hospitalized on November 10, 1956 for the first episode of congestive heart failure; he improved after digitalization. His past history includes hypertension averaging 180/100 mm. Hg. and angina pectoritis which required nitroglycerine only occasionally. He had had mild diabetes mellitus for about fifteen years. There is no history of myocardial infarction.

The electrocardiogram in the illustration was taken on December 14, 1956 and subsequent tracings are quite similar. It is of interest for two reasons:

(1) The pulses bigemini shown in Lead II was found to occur frequently and could be induced by emotionally threatening problems. For example, with a patient attached to the electrocardiogram, a pleasant chat showed no arrhythmia. As the blood sugar report was brought into the room, producing an unpleasant look on the physician's countenance, bigeminal rhythm would appear and would last until the patient was reassured. This was repeated on eight occasions with the same results. While this is not proof, it is clinically suggestive and illustrates an old observation that premature beats (usually not coupled, however) are often emotionally precipitated.

(2) The electrocardiogram shows left axis deviation. The width of the QRS complexes is usually 0.11 seconds and occasionally 0.12 seconds. There is slurring of the ascending and descending limbs of the QRS complexes, espe-





cially well seen in Leads V1 and V2. (Some of the QRS complexes have been retouched for illustration purposes). The limb leads superficially suggest left bundle branch block with the broadened S waves in Leads V4—V6. Right ventricular hypertrophy would be considered because of the tall R waves in Leads VI—V3.

The vectorcardiogram (taken by the modified cube system of Grishman) clearly shows that the resultant vectors are directed to the right and posteriorly (well seen in the horizontal plane) and superiorly (well seen in the frontal and sagittal planes). The author has shown that this occurs when a large anterolateral or more often posterolateral myocardial infarct diminishes the electromotive forces generated by the left ventricle. Thus, the infarction vectors point to the right and superiorly accounting for the tall R waves in Leads aVR and VI—V3, which leads face the positive side of the QRS vector loop. From the pattern standpoint, tall R waves in Leads aVR and the right precordial leads are strongly suggestive of this type of large infarction. There is no evidence in the vectorcardiogram of a block in the main conduction bundles so that this tracing is neither right nor left bundle branch block; nor is there evidence of right ventricular hypertrophy.

Similar conclusions may be reached by employing Grant's method of analysis: the initial 0.04 second vector of the QRS complex is at an axis of almost plus 115 degrees, while the terminal 0.04 second vector is at an axis of minus 95 degrees. The angle between these two vectors is 210 degrees, while in the normal heart it is under 100 degrees. According to Grant, when, in left axis deviation, the angle between the initial and terminal 0.04 second vectors exceeds 100 degrees, peri-infarction block in myocardial infarction is present. He believes it is due to a block in the major branch of the left conduction bundle. Certainly the circuitousness of the horizontal plane QRS vector loop suggests prolongation in the transmission of the depolarization forces in the left ventricle and explains the slurring and the prolongation of the terminal 0.04 seconds of the QRS complexes.

This electrocardiogram is considered to be an example of a large diaphragmatic (inferior) and lateral wall myocardial infarct with digitalis effect.

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## Case Report Section

### Diffuse Interstitial Fibrosis of the Lungs\* (Hamman-Rich Syndrome) Successful Palliation of a Case with Steroid Therapy

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In 1944 Hamman and Rich<sup>1</sup> described four cases of a unique type of diffuse interstitial fibrosis of the lungs, which they considered to be an entity not previously described. Since then (through June, 1956) 36 cases of the Hamman-Rich Syndrome, as it has come to be known, have been reported,<sup>2</sup> all except one ending in death<sup>3</sup>. The average age at the time of onset of the disease has been 44.5 years, varying from 13 to 72 years, and the average duration of the disease has been two years from the onset of symptoms. The chief and paramount symptom has been dyspnea, usually all out of proportion to the extent of the pulmonary lesions demonstrated by x-ray films. Other symptoms have been inconsistent, but have included cough, cyanosis, fatigability, ankle edema, and those findings usually associated with right heart failure.

On physical examination there are no characteristic findings. Reported have been dyspnea, cyanosis, finger clubbing and fever, as well as signs of cardiac failure and pneumonia.

Laboratory examination has been consistently helpful only insofar as the chest roentgenogram is concerned. All patients have had diffuse bilateral opacities, varying from strandlike to patchy to nodular. Sputum has been negative for tubercle bacilli in all, but the tuberculin reaction has been positive in about one-half of the cases. Polycythemia has been a feature in a few. The EKG has shown evidence of cor pulmonale in 11 instances (30 per cent) with autopsy findings showing right ventricular hypertrophy in 18 (50 per cent). Multiple biochemical determinations have shown no consistent pattern.

Pathologically, the lesions have been fairly specific. The tissue in the great majority of cases has been obtained at autopsy, but in a few by lung biopsy. Opportunities for both sources have been afforded in a few. The findings include (1) Proliferation of the alveolar lining cells—with cuboidal and even columnar cells present (2) Necrosis of alveolar and bronchial epithelium. (3) Hyaline membrane formation around the alveoli. (4) Marked edema of the alveoli. (5) Extensive interstitial fibrosis. (6) Marked perivascular fibrosis. (7) Eosinophilic interstitial infiltration. (8) No demonstrable etiology.

Therapeutically, practically all of the antibiotics and antituberculosis drugs have been tried with a marked lack of success. A few have re-

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sponded to steroid therapy for a short time, with one report describing a patient that maintained improvement, both clinically and roengenographically, for at least 17 months.<sup>3</sup> The diagnosis in this case had been made by lung biopsy. In at least two other cases early improvement occurred with steroid therapy, but a rapidly fatal outcome ensued on withdrawal of the medication.<sup>4, 5</sup>

It is the purpose of this paper to report a case of diffuse interstitial fibrosis (Hamman-Rich Syndrome) diagnosed by lung biopsy, with achievement of symptomatic and objective improvement on steroid therapy over a period of at least three years (the patient is still alive).



FIGURE 1

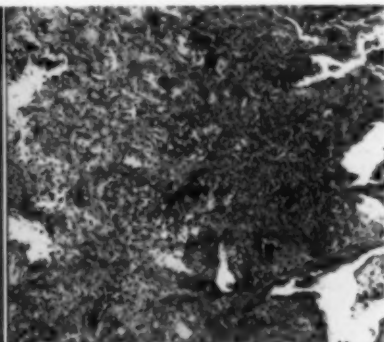


FIGURE 2

*Figure 1:* Radiograph, taken on admission to the hospital, demonstrating prominent bronchovascular markings, plus scattered peribronchial infiltration and fibrosis, and cardiac enlargement (cardio-thoracic ratio 14/26.7).—*Figure 2:* Photomicrograph, 130x. Low power photograph of section of lung biopsy specimen, showing marked fibrosis with almost complete obliteration of alveoli in this area, and a focus of lymphocytic infiltration.

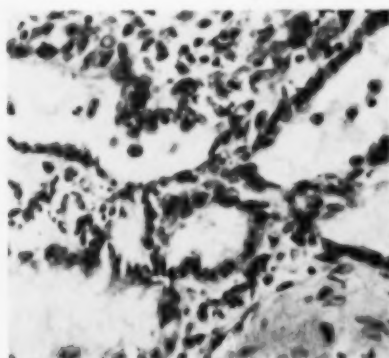


FIGURE 3

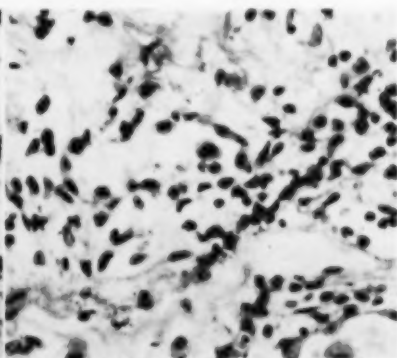


FIGURE 4

*Figure 3:* Photomicrograph, 480x. High power photograph of section of lung biopsy specimen demonstrating cuboidal to columnar alveoli lining cells, some with cilia.—*Figure 4:* Photomicrograph, 480x. High power photograph of section of lung biopsy specimen, showing edema, and infiltration of lymphocytes, plasma cells, and eosinophils.

HCT, a 55 year old college professor entered the hospital with a complaint of shortness of breath. He had first noticed the shortness of breath some six months before following a strenuous game of tennis, which he played habitually. A few weeks later he noticed increasing shortness of breath while climbing stairs, lecturing, or even walking up a low hill on his way to class. At this time he sought medical care from his personal physician and a diagnosis of bronchopneumonia was made. When treatment with various antibiotics proved of no avail, he was thought possibly to have heart failure, although clinical signs did not substantiate this diagnosis, and was treated with digitalis and mercurial diuretics, but without noticeable improvement. He was then admitted to the Moses H. Cone Memorial Hospital. Further history revealed there had been a 10 lb. weight loss, but that he had had no cough, pain, sputum, hemoptysis, night sweats, edema, urinary or defecatory abnormalities, or other symptoms. The only previous hospitalization had been for appendectomy about a year prior to the present admission. He was an artist, inclined to be morose, secretive, apprehensive, and non-communicative. He was married and had one child.

**Physical Examination:** Temperature 100.4°F, Pulse 90/min., BP 110/80 mm. Hg., Respiration 22/min. He did not appear to be ill; there was no abnormality of the head, including the eyes, ears, nose and throat, or the neck. To percussion the lungs were normal. On auscultation there were rales at the right base posteriorly, extending up about three inches, with some diminution of expansion on the right side. There were a few rales at the left base posteriorly just above the diaphragm. The heart seemed to be enlarged to the left, but had a regular rate and rhythm, and no thrills. The abdomen was negative, as were the genitalia, rectum, lymph nodes, and extremities.

**Laboratory Examination:** RBC 4.2 million, Hgb. 12.5 grams, WBC 7,800 with 6 per cent eosinophils, 4 monocytes, 21 lymphocytes, 69 polymorphonuclears. Urinalysis (including test for Bence-Jones protein) and stool examination were negative. Total serum protein was 6.6 mgm. per cent with an A/G ratio of 0.915 (3.15/3.45). The various agglutinations were negative. The BSP test showed 12 retention in 45 minutes. The serum potassium was 4.98 mEq./l. The CO<sub>2</sub> was 30 mEq./l, chlorides 99 mEq./l. The urea nitrogen was 19.2 mgm. per cent, the alkaline phosphatase 5.6 Bodansky units. The cephalin flocculation showed one plus in 24 hours, three plus in 48 hours. Blood culture was negative. An x-ray film of the chest (Fig. 1) was interpreted to show some type of chronic pathology involving principally the lower half of each lung field (prominence of the bronchovascular markings and scattered peribronchial infiltration, with some degree of fibrosis). The heart was slightly enlarged with a cardio-thoracic ratio of 14/26.7. X-ray films of the hand, taken because of the possibility of sarcoid, showed no abnormality. Various skin tests, including tuberculin, produced no reaction.

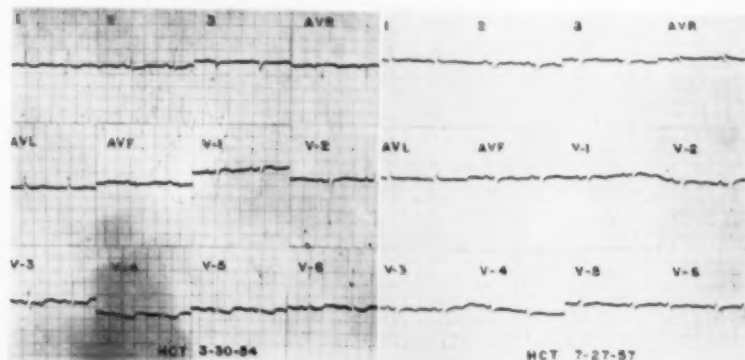


CHART 1

CHART 2

**Chart 1:** Initial EKG, taken 3-30-54, before institution of any therapy. Notice in Lead (1) T-sagging; Lead (2), R present, ST-T slightly depressed; Lead (3), small QRS, S greater than R; AVR, biphasic T; AVL, P upright; AVF, QRS low voltage; V-1, normal; V-2, S deep; V-3, R prominent, T biphasic; V-4, R upright, T sagging; V-5 and V-6, normal.—**Chart 2:** Latest EKG, taken 7-27-57. Lead 1 shows nodal extrasystoles; Lead 2, small R, S deep, ST-T normal; Lead 3, S very deep, occasional PVC; AVR, R present, occasional PVC; AVL, P biphasic; AVF, S deep; V-1, normal; V-2, S deep; V-3, T upright; V-4, small R, S deep; V-5 and V-6, normal.

Venous pressure and circulation time were normal. The EKG was interpreted as showing a definitely abnormal record suggesting pericardial and/or myocardial damage. (EKG Chart No. 1)

As no definite diagnosis could be reached on these findings, scalene node biopsy was proposed. Just prior to this operation his temperature rose to 102°F, and there were palpable shotty nodes in the neck, both axillae, and the inguinal areas. A node was removed from the left posterior cervical triangle: the pathological diagnosis was lymphatic hyperplasia, etiology unknown. Three days later a diagnostic thoracotomy was performed at the right middle lobe area. Palpation revealed a diffuse fibrosis with some nodulation throughout the lung. The lung would not collapse, and a large amount of it did not appear to be aerated. A small wedge of the lower lobe was resected for study.

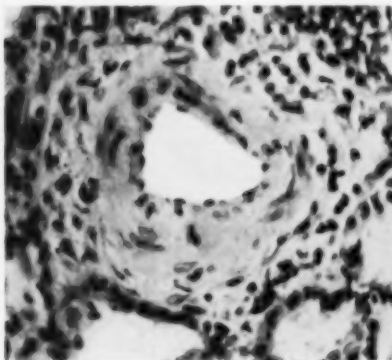


FIGURE 5



FIGURE 6

*Figure 5:* Photomicrograph, 480x. High power photograph of section of lung biopsy specimen demonstrating proliferative reaction around one of the smaller pulmonary vessels.—*Figure 6:* Radiograph taken 3 months after lung biopsy, and initiation of steroid therapy. There has been a decrease in the peribronchial markings, and the cardio-thoracic ratio is 13/26.



FIGURE 7

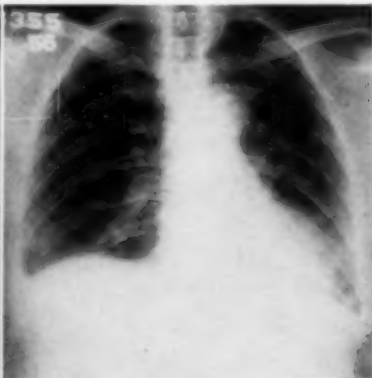


FIGURE 8

*Figure 7:* Radiograph taken one year after initiation of therapy. The fibrosis is still less than it was nine months before (Fig. 6), and the cardio-thoracic ratio is 12.5/26.—*Figure 8:* Radiograph taken 2 years after initiation of therapy. There has been no change in the fibrosis or heart size within the past year.

Pathological Report (H. Z. Lund, M.D.): Received fresh is a partially collapsed portion of lung measuring 6 x 6 x 1.5 cm. There is moderate anthracosis. On section there are irregular poorly defined gray foci scattered throughout the tissue. Some mucin is present on the cut surface. Microscopically there is marked interstitial fibrosis with obliteration of all but a few alveoli (Fig. 2). The alveoli seen have enlarged lining cells most of which are cuboidal, but conspicuous in areas are alveolar spaces lined by tall columnar epithelium which is in part ciliated (Fig. 3). This is mucin producing. Occasionally this epithelium protrudes as small papillae, and at other places it is interrupted by foci of squamous metaplasia. There is edema and a marked infiltration of lymphocytes, plasma cells and eosinophils (Fig. 4). There is proliferative endarteritis and endophlebitis, occasionally with complete obliteration of the lumen (Fig. 5).

**Diagnosis:** This is a type of interstitial pneumonitis. The fibrosis has not gone on to the usual degree seen in Hamman-Rich syndrome, but this is probably an earlier more exudative stage.

In view of this diagnosis, he was placed on intramuscular corticotropin gel, 40 units daily for three days, then 20 mgm. daily for three days, followed by 10 mgm. daily. He was discharged on 10 mgm. twice a week, and was soon able to return to work. He has been able to continue working without significant impairment for the past three years. He still gets short of breath with strenuous exercise, but is able to walk and take moderate exercise without difficulty. Serial chest x-ray films (Fig. 6, 7 and 8) have shown a decrease in the size of the heart. Serial EKG's have shown the following changes: (1) Increased evidence of left axis shift, although the x-ray film shows less evidence of left heart enlargement; (2) Occurrence of premature ventricular contractions, which were not present at first, and (3) Less evidence of myocardial damage as evidenced by more normal T-Waves. (The most recent EKG is shown in Chart 2).

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# Chronic Tracheopathia Osteoplastica

## A Case Report

JOHN W. POLK, M.D., F.C.C.P.\*

Springfield, Missouri

and

JOSE A. CUBILES, M.D.\*\*

Mt. Vernon, Missouri

Tracheopathia osteoplastica as defined by Carr and Olsen,<sup>1</sup> is a rare disease of the trachea and bronchi. It is characterized by growths of cartilage and bone within the wall of the trachea or bronchus that project into the lumen. These may be in the form of sessile polyps or plaques. If the growths become excessive they may partially obstruct the lumen of the tracheobronchus. The clinical symptoms are cough, expectoration, hemoptysis, fever and episodes of pneumonitis. The symptoms vary in intensity, depending upon the extent of involvement and the degree of obstruction. In 1857 Wilks<sup>2</sup> first described this disease. Many case reports have been presented since that time. Dalgaard<sup>3</sup> had reviewed the literature and established 90 authentic cases in 1947. Carr and Olsen<sup>4</sup> in 1950 presented seven cases in Mayo Clinic.

The purpose of this report is to establish another case diagnosed by bronchoscopy and present several features of this case which we feel are unusual.

This 41 year old white man states he was well until the middle of March, 1954, when he had chest pain on the left side, cough, expectoration of semipurulent material and fever and chills. He was a student at one of the local colleges and was diagnosed by the school physician as having pneumonia. An x-ray film dated March 31, 1954, revealed atelectasis of the lingula. He was advised to seek bronchoscopy and admission to the Missouri State Sanatorium. On April 17, 1954, bronchoscopy was performed, as an out-patient. At the superior margin of the trachea on the left side a projection of firm irregular tissue began and extended through the entire length of the trachea. This tissue presented itself in shelf-like fashion. A biopsy taken from the inferior portion of this was noticed to be hard and partly calcified. Visualization of the lingula bronchus failed to reveal any obstruction which would account for the atelectasis. The remainder of the tracheobronchial tree was normal.

He was then admitted to the Missouri State Sanatorium April 22, 1954. At this time the atelectasis in the lingula division of the left lung had cleared but since no positive diagnosis had been made, rebronchoscopy was advised. On May 25, 1954, bronchoscopy was repeated. The same pathological findings were present. The pathological diagnosis of chronic tracheopathia osteoplastica was established by biopsy. Because no specific therapy was indicated he was discharged and instructed to have recheck bronchoscopy every six months.

On August 9, 1954, bronchoscopy was repeated and again no additional findings noted. He developed a severe upper respiratory infection in September, 1955, with cough, hemoptysis, fever and chills and was re-admitted to the Missouri State Sanatorium on October 3, 1955. Bronchoscopy was repeated on October 5, 1955, when the lesion previously noted was again observed but further calcification and ossification had occurred with almost complete fixation of the left side of the trachea. Purulent secretions were noted in both bronchial systems. These were aspirated and cultures for sensitivity made.

At the time of this admission he was placed on alevair inhalation every four hours with vaponephrine drops included in the inhalation. Nasal oxygen was given *Pro re*

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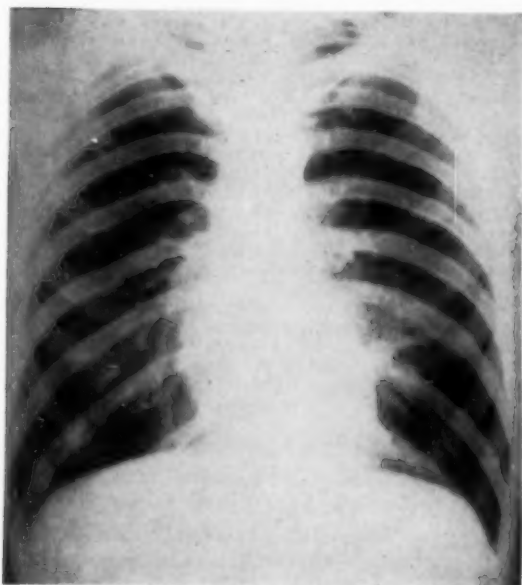


FIGURE 1: Shows atelectatic area in the lingula of the lung.

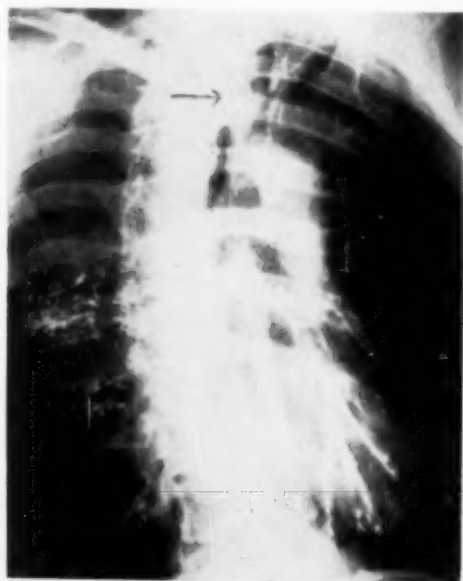


FIGURE 2: Tracheogram showing thickening and rough edges in trachea.

nata. Penicillin was administered twice daily for three days. On this routine he improved remarkably and was discharged October 13, '955.

He has had two episodes of obstructive pneumonitis since discharge. For the first of these which occurred in February, 1956, he was treated with broad spectrum antibiotics and prednisolone, 5 mgm. three times a day for five days. His symptoms of this episode completely abated and he had no further pulmonary symptoms until July 10, 1957. At this time he developed upper respiratory infection, cough, productive sputum, and a feeling of tightness in the upper anterior chest. Broad spectrum antibiotics were again prescribed for five days. On August 9, 1957, bronchoscopy was again repeated at St. John's Hospital, Springfield, Missouri. The previously described calcified growths along the left side of the trachea were again noted. For the first time, however, the calcified polyp-like growths were noted in the right primary bronchus and the bronchus intermedius of the posterior wall. Biopsy of these again was performed and the previously established diagnosis supported. He has now returned home with instructions to take postural drainage and ammonium chlorides during the winter months. He is to receive antibiotics from his local physician for three days each month rotating the antibiotics to prevent the emergence of resistant organisms.

We wish to express our appreciation to Dr. David F. Gorelick and Dr. Fred C. Collier, consultant pathologists of the Missouri State Sanatorium. We also wish to express our appreciation to Dr. William E. Taylor of the Southwest Missouri State College.

#### COMMENT

Carr and Olsen<sup>1</sup> discussed the hypothesis as to the pathogenesis of tracheopathia osteoplastica and state that none of these have been proved. They considered the most acceptable of these hypotheses to be Dalgaard's concept, in which the undifferentiated connective tissue cells in the wall of the trachea and bronchi develop into cartilage cells that grow into islands of cartilage, eventually becoming calcified. The invasion of the connective tissue is rich in blood vessel formation which results in the formation of marrow cavities lined with osteoblasts. This may account for the transformation into bone. It should be noted that for three years the disease in this patient was noted to be confined to the trachea. In

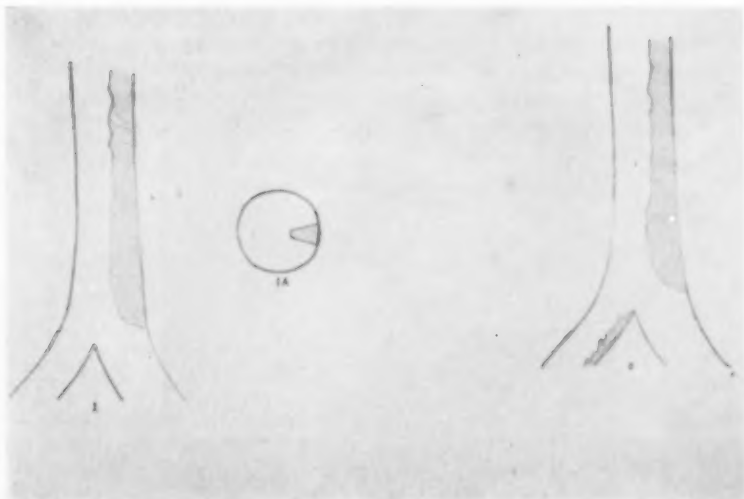


FIGURE 3: (1) Schematic drawing of trachea. (1A) As seen through bronchoscope, 1955. (2) Schematic drawing showing extension into the right primary bronchus, 1957.

six bronchoscopies, all performed by the same individual (J.W.P.), no lesion had been found extending beyond the trachea. On the seventh bronchoscopy of August 9, 1957, involvement of the right primary bronchus and bronchus intermedius was noted. At the time of first bronchoscopy on April 17, 1954, the patient had an atelectasis of the lingula demonstrated by chest x-ray film but no obstruction could be found in the lingula bronchus.

The patient has now received broad spectrum antibiotics and prednisolone therapy on two occasions. An accurate evaluation of the benefit of the cortisone cannot be ascertained but symptomatic relief was prompt and effective. We feel that it is entirely possible, however, that the prednisolone and antibiotics might relieve some of the inflammatory reaction throughout the tracheobronchial tree and that in extremely severe cases of this disease its use would be well warranted. We would also stress the use of postural drainage, expectorants and bronchodilators in the treatment of this disease.

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## Editorial

### Results of Drug Treatment of Non-Hospitalized Tuberculous Patients Compared with Those Immediately Hospitalized

A great deal has been written about the drug treatment of nonhospitalized patients with tuberculosis. It is worth while, therefore, to compare the results from this type of program with the results obtained from immediate hospitalization of over 500 consecutive patients and the use of controlled drug therapy, tomographs, bronchoscopy plus early resection when indicated. In the treatment program used in New York City, a combination of two drugs was given. We have used all three drugs concurrently and continuously. They indicate toxic reactions necessitating a change in drug combination in 4 per cent of patients treated. In our experience, toxic reactions to isoniazid occur in 1 per cent, to streptomycin in over 2 per cent and to PAS in over 10 per cent. They report x-ray improvement in 50 per cent of their patients and 12 per cent show deterioration. The only worsening that we see occurs in patients with associated disease and bronchogenic carcinoma is the most common, being found in over 1 per cent. New York City's few toxic reactions and the poor rate of clearing seen on x-ray film have but one explanation: the patients do not take their drugs.

At the end of 24 months of drug therapy, they report that 83 per cent of minimal cases, 60 per cent of moderately advanced and 40 per cent of far advanced cases have negative sputum culture. In our hospital, all cases of minimal and moderately advanced pulmonary tuberculosis were negative on gastric culture and only 2 per cent of the far advanced were left as chronics. Thus, 48 per cent of their patients would be classified as "arrested" according to National Tuberculosis Association standards, 12 per cent are "arrested with residual cavitation" and 40 per cent are still positive. Under our treatment regimen, 92 per cent of patients have negative gastric cultures and stable x-ray films in an average period of hospitalization of 212 days, 3 per cent die from tuberculosis, 3 per cent die from associated disease and 2 per cent are left as chronics. These chronic cases would qualify as "arrested with cavitation" by New York's standards since they have reached the point where they deny sputum but are positive on gastric culture; after a few months sputum returns and is positive first on culture and then on smear when resistant organisms appear. A large percentage of their cases designated as "arrested with residual cavitation" will reactivate and when they do, they will fall into the category of chronic tuberculosis with organisms resistant to the major drugs so they are no longer candidates for resection. They report that 45.4 per cent of their patients positive at the end of one year have isoniazid resistant organisms. They also report that there has not been a marked increase in the per-

centage of isoniazid and streptomycin resistant organisms among their new cases, but this does not mean that the patients with resistant organisms are not contagious—it means only that a significant number of their contacts have not had time enough to develop reinfection type tuberculosis.

If we had used only clinic visits for follow-up of our patients we would have missed more than half of those who reactivated—these were picked up by gastric cultures when the patients returned to the hospital a year after discharge and six months after stopping drug therapy. Their patients are not allowed to work, so they and their families are dependent upon welfare, a minimum of two years for those who become negative and the rest of their lives for the 40 per cent who stay positive. Our patients and their families receive welfare only for the 212 days of hospitalization since they return immediately upon discharge to their former occupations regardless of physical activity.

Thus, drug therapy of nonhospitalized tuberculosis patients falls far short in every respect of what can be achieved with immediate hospital care. Outpatient treatment has a relatively low percentage of conversion of sputum cultures and, if sputum is denied, they are automatically considered negative, which is definitely not so. An alarmingly high percentage of consistently contagious cases will remain as chronics. The low incidence of toxic drug reactions and the fact that only 50 per cent of patients show chest x-ray film improvement, indicate that the patients do not take their drugs. Because of the great number of chronic cases this program is not economical either in restoring to normal productive life or in saving the tuberculosis funds. This type of program is contrary to every basic idea of public health. It does not decrease the tuberculosis problem today and assures us of an even greater problem within the next few years because there will be an ever increasing number of patients with resistant organisms as a result of contact with these open cases.

Drug treatment of nonhospitalized patients with tuberculosis, therefore, falls far short in every respect of what can be achieved with immediate hospital care.

ALBERT R. ALLEN, M.D., F.C.C.P.  
Selah, Washington

## College Chapter News

### CANARY ISLANDS CHAPTER

The Canary Islands Chapter held its fall meeting in Santa Cruz de la Palma on October 23. A round table discussion on Cardiorespiratory Function was presented with Dr. J. M. del Arco Montesinos of Santa Cruz as moderator. Drs. A. Bosch Millares, E. Gonzalez Gonzalez, and A. Mendes de Lugo participated in the discussion.

### WESTERN INDIA CHAPTER

The Inaugural meeting of the Western India Chapter was held at St. George's Hospital, Bombay, on August, 29. Dr. Bomy R. Billimoria, Governor of the College for Western India, presided and opened the proceedings. The following officers were elected:

President:	Rustom Jal Vakil, Bombay
Vice-President:	S. G. Dhanik, Surat
Vice-President:	S. C. Sheth, Bombay
Vice-President:	V. M. Bahulkar, Poona
Secretary-Treasurer:	Jer K. Lashkari, Bombay

### PUERTO RICO CHAPTER

The Puerto Rico Chapter held its second scientific session this year on June 8 at the Cayey Tuberculosis Hospital, Cayey, at which time an x-ray diagnostic conference was presented. The third scientific program for 1958 was presented by the chapter on September 7. This meeting was devoted to a series of cases dealing with "The Pulmonary Manifestations of Systemic Diseases."

### NEWS NOTES

**Dr. George R. Herrmann**, Galveston, Regent of the College, who is the first Honorary Professor of Medicine at the University of Puebla, Mexico and Professor of Medicine, University of Texas, participated in the First Congress of Medicine and Surgery held at the University of Puebla, Puebla, Mexico, July 13-19.

**Carl W. Tempel**, former commanding officer of the Valley Forge Army Hospital, Phoenixville, Pennsylvania, has been promoted to Brigadier General and has been appointed Chief of the Professional Division, Department of the Army, Washington, D. C.

**Dr. Jesse E. Douglass**, formerly of the Minnesota State Sanatorium at Ah-gwah-Ching, has been appointed Medical Director of the Mineral Springs Sanatorium, Cannon Falls, Minnesota.

**Dr. Arthur Q. Penta**, Schenectady, New York, recently returned from an extended trip through South America. While in Rio de Janeiro, Brazil, Dr. Penta attended the meeting of the Pan-American Bronchoesophagological Association and was the guest speaker before a combined meeting of the Rio de Janeiro Chapter of the College and the members of the staff of San Miguel Hospital. In Santiago, Chile, Dr. Penta was guest lecturer at the Postgraduate Course on Diseases of the Chest sponsored by the Graduate School of Medicine, University of Chile.

**Dr. Burton L. Zohman**, Brooklyn, New York, has been appointed Clinical Professor of Medicine at the State University College of Medicine at Brooklyn.

**Dr. Merle W. Moore**, Portland, Oregon, was recently elected President of the American College of Allergists.

**Dr. Jean Chenebault**, Casablanca, Morocco, served as President of the Organization Committee of the Moroccan Medical Conference and delivered the welcoming address in Rabat on May 15.

**COLLEGE INTERIM SESSION**  
**and**  
**SEMI-ANNUAL MEETING, BOARD OF REGENTS**

The Interim Session of the College will be held in Rochester, Minnesota, November 29, 30 and the morning of December 1. Headquarters will be at the Kahler Hotel. The scientific sessions will take place in Plummer Hall and Mann Hall of the Mayo Clinic Buildings. Fireside Conferences will be held in the Mayo Foundation House. There will also be tours of the Mayo Clinic, technical exhibits, motion pictures, round table luncheons, a banquet and dancing. The semi-annual meeting of the Board of Regents will be held in Minneapolis at the Radisson Hotel on December 1. The Board meeting will be followed by a dinner and scientific session on inhalation therapy.

**Interim Session Program**

**SATURDAY, NOVEMBER 29**

**Morning Session**

**7:30 a.m.—Thoracic and Cardiovascular Surgery**

O. Theron Clagett, Professor of Surgery, Mayo Foundation, Rochester, Minnesota—**Methodist Hospital**

John W. Kirklin, Associate Professor of Surgery, Mayo Foundation, Rochester, Minnesota—**St. Mary's Hospital**

Dwight C. McGoon, Instructor in Surgery, Mayo Foundation, Rochester, Minnesota—**St. Mary's Hospital**

**9:00 a.m.—Registration, Kahler Hotel Mezzanine**

Technical exhibits will be open adjacent to the registration area. A door prize will be given by the Weber and Judd Drug Company of Rochester, Minnesota, to a lucky college member registering at these exhibits. Free coffee, sweet rolls and cokes will be served in this area.

E. Fougere and Company

Eli Lilly and Company

McNeil Laboratories, Inc.

V. Mueller and Company

Mist O<sub>2</sub> Gen Equipment Company

George P. Pilling and Son

Searle and Company

E. R. Squibb & Son

Thompson Engineering  
Products Co.

The George Waters Company

Winthrop Laboratories

Wyeth Laboratories

**9:00 a.m.—Motion Picture Session, Centennial Hall, Kahler Hotel  
Mezzanine (also to be shown at 2:00 p.m. Saturday, 9:00 a.m.  
& 2:00 p.m. Sunday, and 9:00 a.m. Monday)**

**9:00 a.m.—RESUSCITATION FOR CARDIAC ARREST**

Claude S. Beck, University Hospitals, Cleveland, Ohio (19 minutes)

**9:24 a.m.—SURGICAL REMOVAL OF MYXOMA OF THE LEFT AURICLE SIMULATING  
MITRAL STENOSIS**

Denton A. Cooley and George C. Morris, Jr., Baylor University College of Medicine, Houston, Texas. (15 minutes)

**9:44 a.m.—ACTION OF THE HUMAN HEART VALVES**

Karl P. Klassen and C. V. Meckstroth, Ohio State University Health Center, Columbus, Ohio. (20 minutes)

**10:09 a.m.—COCCIDIOIDOMYCOSIS, ITS EPIDEMIOLOGIC AND CLINICAL ASPECTS**

Libero Ajello and Roger Egeberg, directed by Mr. Graham Heid, Public Health Service & Veterans Administration, Washington, D.C. (19½ minutes)



**Motion Picture Session (continued)****10:34 a.m.—PRINCIPLES OF RESPIRATORY MECHANICS**

Jere Mead, E. P. Radford, Jr., M. B. Mellroy, B. G. Ferris, Jr. and J. L. Whittenberger, Department of Physiology, Harvard Medical School, Boston, Massachusetts. (22 minutes)

**11:01 a.m.—THE USE OF A GASTRIC TUBE TO REPLACE OR BY-PASS THE ESOPHAGUS**

Henry J. Heimlich, New Rochelle, New York. (30 minutes)

**11:36 a.m.—TREATMENT OF THORACIC INJURIES**

Rudolph J. Noer, Louisville, Kentucky. (31 minutes)

**9:00 a.m.—Tour of Clinic**

- A. Clinic Buildings
- B. Medical Sciences Building

**Afternoon Session****Scientific Session, Pulmonary Section—Plummer Hall, Mayo Clinic-Plummer Building**

*Chairman:* R. Drew Miller, Assistant Professor of Medicine, Mayo Foundation, Rochester, Minnesota

*Co-chairman:* Seymour M. Farber, Associate Clinical Professor of Medicine, University of California School of Medicine, San Francisco, California

**2:00 p.m.—Newer Developments in the Chemotherapy of Tuberculosis**

Martin J. FitzPatrick, Associate Professor of Medicine, University of Kansas School of Medicine, Kansas City, Kansas

**2:30 p.m.—Current Standards for Surgical Therapy of Tuberculosis**

John B. Grow, Assistant Professor of Surgery, Colorado University School of Medicine, Denver, Colorado

**3:00 p.m.—A Serologic Test for Diagnosis of Tuberculosis**

Guy P. Youmans, Professor and Chairman, Department of Bacteriology, Northwestern University Medical School, Chicago, Illinois

**3:30 p.m.—Surgery of the Trachea and Bronchi**

Donald L. Paulson, Clinical Associate Professor of Thoracic Surgery, Southwestern Medical School, University of Texas, Dallas, Texas

**4:00 p.m.—Recent Developments in the Management of Fungus Diseases**

Michael L. Furcolow, Associate Clinical Professor of Internal Medicine, University of Kansas Medical Center, Kansas City, Kansas

**4:30 p.m.—Recent Evaluations of Sarcoidosis**

Harold L. Israel, Associate Professor of Medicine, University of Pennsylvania Graduate School of Medicine, Philadelphia, Pennsylvania

**Scientific Session, Cardiac Section—Mann Hall, Medical Sciences Building**

*Chairman:* Raymond D. Pruitt, Professor of Medicine, Mayo Foundation, Rochester, Minnesota

*Co-chairman:* David H. Waterman, Attending Thoracic Surgeon, University of Tennessee Memorial Research Center and Hospital, Knoxville, Tennessee

**2:00 p.m.—Clinical Manifestation of Several Types of Tricuspid Valvular Disease**

Oglesby Paul, Clinical Associate Professor of Medicine, University of Illinois College of Medicine, Chicago, Illinois

**Saturday, November 29 (continued)****2:30 p.m.—Femoral Artery Blood Flow**

D. J. Ferguson, Associate Professor of Surgery, University of Minnesota, Minneapolis, Minnesota

**3:00 p.m.—Hypothermia for Intracardiac Surgery**

F. John Lewis, Professor of Surgery, Northwestern University School, Chicago, Illinois

**3:30 p.m.—Diagnostic Application of Indicator-Dilution Curves using a Central Sampling Technic**

H. J. C. Swan, Assistant Professor of Physiology, Mayo Foundation, Rochester, Minnesota

**4:00 p.m.—Experience with Chlorothiazide in the Management of Hypertension**

Robert L. Grissom, Professor and Chairman, Department of Internal Medicine, University of Nebraska College of Medicine, Omaha, Nebraska

**SATURDAY EVENING, NOVEMBER 29****6:00 p.m.—Cocktails, Regency Room and University Club Lounge, Kahler Hotel**

Courtesy of Minnesota Chapter, American College of Chest Physicians

**7:00 p.m.—Banquet, Elizabethan Room, Kahler Hotel**

Donald R. McKay, Buffalo, New York, President, American College of Chest Physicians, presiding

**9:00 p.m.—Dancing, Royal Coach Room, Kahler Hotel****SUNDAY, NOVEMBER 30****9:00 a.m.—Motion Picture Session, Centennial Hall, Kahler Hotel Mezzanine, (also to be shown at 2:00 p.m. Sunday)****9:00 a.m.—Technical exhibits, Kahler Hotel Mezzanine****10:00 a.m.—Tours of Medical Buildings in Rochester****12:45 p.m.—Round Table Luncheons****1) DISORDERS OF ESOPHAGEAL MOTILITY**

*Moderator:* Charles F. Code, Professor of Physiology, Mayo Foundation, Rochester, Minnesota

*Panelists:* N. C. Hightower, Scott and White Clinic, Temple, Texas  
E. Clinton Texter, Jr., Assistant Professor of Medicine, Northwestern University Medical School, Chicago, Ill.  
C. Allen Good, Professor of Radiology, Mayo Foundation, Rochester, Minnesota

**2) BRONCHOGRAPHY, INDICATIONS AND TECHNIQUES**

*Moderator:* Sheldon E. Domm, Attending Thoracic Surgeon, University of Tennessee Memorial Research Center and Hospital, Knoxville, Tennessee

*Panelists:* André Mackay, Assistant Professor of Medicine, University of Montreal Faculty of Medicine, Montreal, P. Q.  
Chauncey N. Borman, Clinical Assistant Professor of Radiology, University of Minnesota, Minneapolis, Minn.  
Albert H. Andrews, Jr., Associate Clinical Professor of Bronchoesophagology, University of Illinois College of Medicine, Chicago, Illinois

**Round Table Luncheons (continued)****3) SURGICAL TREATMENT OF ACQUIRED VALVULAR HEART DISEASE**

*Moderator:* Robert P. Glover, Assistant Professor of Clinical Surgery, University of Pennsylvania Medical School, Philadelphia, Pennsylvania

*Panelists:* Richard L. Varco, Professor of Surgery, University of Minnesota Medical School, Minneapolis, Minnesota

John W. Kirklin, Associate Professor of Surgery, Mayo Foundation, Rochester, Minnesota

F. John Lewis, Professor of Surgery, Northwestern University Medical School, Chicago, Illinois

**4) EARLY DETECTION OF EMPHYSEMA**

*Moderator:* Peter A. Theodos, Associate in Medicine, Jefferson Medical College, Philadelphia, Pennsylvania

*Panelists:* George R. Meneely, Associate Professor of Medicine, and Assistant to Dean, Vanderbilt University School of Medicine, Nashville, Tennessee

John Rankin, Assistant Professor of Medicine, University of Wisconsin Medical School, Madison, Wisconsin

H. O. Peterson, Professor of Radiology, University of Minnesota Medical School, Minneapolis, Minnesota

**Scientific Session, Plummer Hall, Mayo Clinic-Plummer Building**

*Chairman:* Herman J. Moersch, Professor of Medicine, Mayo Foundation, Rochester, Minnesota

*Co-Chairman:* John F. Briggs, Clinical Associate Professor of Clinical Medicine, University of Minnesota Medical School, Minneapolis, Minnesota

**2:30 p.m.—Intrathoracic Complications of Subphrenic Infection**

David P. Boyd, Thoracic Surgeon, New England Baptist and New England Deaconess Hospitals, Boston, Massachusetts

**3:00 p.m.—Clinical Application of the Carbon Monoxide Method of Estimating Diffusion Capacity of the Lungs**

David W. Cugell, Assistant Professor of Medicine, Northwestern University Medical School, Chicago, Illinois

**3:30 p.m.—Current Thoughts on Asthma**

John M. Sheldon, Professor of Internal Medicine, University of Michigan Medical School, Ann Arbor, Michigan

**4:00 p.m.—The Staphylococcus: 1959 Nemesis**

Robert J. Anderson, Assistant Surgeon General, U. S. Public Health Service; Chief, Communicable Disease Center, Public Health Service, Atlanta, Georgia

**4:30 p.m.—Current Concepts of Interstitial Pulmonary Fibrosis**

Howard S. Van Ordstrand, Professor of Pulmonary Diseases, Frank E. Bunts Educational Institute, Cleveland, Ohio

**SUNDAY EVENING, NOVEMBER 30****6:00 p.m.—Dutch Treat Buffet, Elizabethan Room, Kahler Hotel****8:15 p.m.—Fireside Conferences, Mayo Foundation House****Subjects and Discussion Leaders****1) THE LUNG IN SYSTEMIC DISEASE**

Robert Carton, Clinical Assistant in Medicine, University of Illinois, Chicago, Illinois

Francis E. Donoghue, Instructor in Medicine, Mayo Foundation, Rochester, Minnesota

Jesse E. Edwards, Professor of Pathology, Mayo Foundation, Rochester, Minnesota

Gordon L. Snider, Assistant Director, Chest Department, Michael Reese Hospital, Chicago, Illinois

**2) PULMONARY FUNCTION TESTS AND THEIR UTILIZATION**

George Bedell, University of Iowa Medical School, Iowa City, Iowa

Ward S. Fowler, Professor of Physiology, Mayo Foundation, Rochester, Minnesota

George A. Saxton, Jr., Associate Professor of Preventive Medicine, University of Illinois Medical School, Chicago, Illinois

**3) CHEMOTHERAPY OF TUBERCULOSIS**

David T. Carr, Assistant Professor of Medicine, Mayo Foundation, Rochester, Minnesota

Sumner S. Cohen, Assistant Medical Director, Glen Lake Sanatorium, Oak Terrace, Minnesota

Hollis E. Johnson, Professor of Clinical Medicine, Vanderbilt University, Nashville, Tennessee

**4) ALLERGY IN PULMONARY DISEASES**

Jacob S. Blumenthal, Clinical Associate Professor of Medicine, University of Minnesota, Minneapolis, Minnesota

Allan Hurst, Assistant Clinical Professor of Medicine, University of Colorado, Denver, Colorado

Louis E. Prickman, Associate Professor of Medicine, Mayo Foundation, Rochester, Minnesota

**5) CARCINOMA OF THE LUNG**

William E. Adams, Professor of Surgery, University of Chicago, Chicago, Illinois

O. Theron Clagett, Professor of Surgery, Mayo Foundation, Rochester, Minnesota

Robert L. Mayoock, Assistant Professor of Clinical Medicine, University of Pennsylvania, Philadelphia, Pennsylvania

**6) DIAGNOSTIC AND SURGICAL METHODS IN INTRACARDIAC SEPTAL DEFECT**

R. O. Brandenburg, Assistant Professor of Medicine, Mayo Foundation, Rochester, Minnesota

Richard L. Varco, Professor of Surgery, University of Minnesota Hospital, Minneapolis, Minnesota

Henry A. Zimmerman, Director of Cardiopulmonary Laboratory, St. Vincent's Charity Hospital, Cleveland, Ohio

**Fireside Conferences (continued)**

- 7) **MEDICAL AND EMOTIONAL REHABILITATION FOLLOWING MYOCARDIAL INFARCTION**  
Howard Burchell, Professor of Medicine, Mayo Foundation, Rochester, Minnesota  
Jay Conger Davis, Assistant Clinical Professor of Medicine, University of Minnesota, Minneapolis, Minnesota  
Ralph Rossen, Director, Psychobiological Division, Mt. Sinai Hospital, Minneapolis, Minnesota  
Richard M. Steinhilber, Consultant in Psychiatry, Mayo Foundation, Rochester, Minnesota
- 8) **TECHNIQUES IN CARDIAC DIAGNOSIS (ROENTGENOLOGIC, CATHETERIZATION, ETC.)**  
Robert Dickerson, Lt. Col. M.C., Chief, Cardiovascular Section, Brooke Army Hospital, San Antonio, Texas  
Joseph Jorgens, Associate Professor of Radiology, University of Minnesota, Minneapolis, Minnesota  
Earl Wood, Professor of Physiology, Mayo Foundation, Rochester, Minnesota
- 9) **SPECIFIC AND NONSPECIFIC THERAPEUTIC APPROACHES TO CONGESTIVE HEART FAILURE**  
Lawrence Coke, Assistant Professor of Medicine, University of Manitoba, Winnipeg, Manitoba  
Stephen R. Elek, Associate Professor of Medicine, University of Southern California, Los Angeles, California  
Robert L. Parker, Associate Professor of Medicine, Mayo Foundation, Rochester, Minnesota

**MONDAY, DECEMBER 1****7:30 a.m.—Mayo Clinic Chest Conference, Diagnostic Problems—  
Mann Hall, Medical Sciences Building**

*Chairman:* Herman J. Moersch, Professor of Medicine, Mayo Foundation, Rochester, Minnesota

**8:30 a.m.—Cardiac Conference—Clinicopathologic Conference—  
Mann Hall, Medical Sciences Building**

*Chairman:* Jesse E. Edwards, Professor of Pathology, Mayo Foundation, Rochester, Minnesota

**9:00 a.m.—Motion Picture Session, Centennial Hall, Kahler Hotel****9:30 a.m.—Thoracic and Cardiovascular Surgery**

F. Henry Ellis, Jr., Assistant Professor of Surgery, Mayo Foundation, Rochester, Minnesota—St. Mary's Hospital

Philip E. Bernatz, Instructor in Surgery, Mayo Foundation, Rochester, Minnesota—Methodist Hospital

**MONDAY, DECEMBER 1**

**CHARTERED BUSES WILL LEAVE FOR MINNEAPOLIS AT 1:00 P.M.  
RESERVATIONS MUST BE MADE IN ADVANCE. PLEASE SEE  
RESERVATION FORM ON PAGE 578.**

**SATURDAY, NOVEMBER 29 — ROCHESTER****8:30 a.m.—Examinations for Fellowship, Coach Room, Kahler Hotel**

The Board of Examiners will conduct oral and written examinations for Fellowship in the American College of Chest Physicians. Candidates are requested to report at 8:30 a.m. at the Coach Room. The written examinations will be held in the morning and the oral in the afternoon. David B. Radner, Chicago, Illinois, Chairman, Board of Examiners.

**9:00 a.m.—Council and Committee Meetings, Kahler Hotel**

Special meetings of councils and committees will be held. The time and place of the meetings will be posted on the hotel bulletin board.

**12:00 noon—Luncheon Meeting, Executive Council, Kahler Hotel**

Donald R. McKay, Buffalo, New York, President

**SUNDAY, NOVEMBER 30 — ROCHESTER****10:00 a.m.—Joint Meeting, Regency Room, Kahler Hotel**

Board of Governors and Board of Regents

Howell S. Randolph, Phoenix, Arizona, Chairman, Board of Governors

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**PROGRAM****Minneapolis, Minnesota****Headquarters: Radisson Hotel****4:00 p.m.—Semi-Annual Meeting, Board of Regents, Room 329**

John F. Briggs, St. Paul, Minnesota, Chairman

**6:30 p.m.—DINNER, Gold Room**

Donald R. McKay, Buffalo, New York, President, American College of Chest Physicians, presiding

**8:00 p.m.—SCIENTIFIC SESSION, Gold Room****Panel Discussion "Inhalation Therapy"**

*Moderator:* Edwin R. Levine, Assistant Professor of Clinical Medicine, Chicago Medical School, Chicago, Illinois

*Panel:* Seymour M. Farber, Associate Clinical Professor of Medicine, In Charge, University of California Tuberculosis and Chest Service, San Francisco Hospital, San Francisco, California

H. Frederic Helmholtz, Jr., Section on Physiology, Mayo Clinic, Rochester, Minnesota

William F. Miller, Assistant Professor of Medicine, University of Texas, Southwestern Medical School, Dallas, Texas

Maurice S. Segal, Clinical Professor of Medicine, Tufts University School of Medicine, Boston, Massachusetts

*Questions and discussion from the floor*

*For hotel accommodations please write direct to:*

**Kahler Hotel, Rochester, Minnesota**

**Radisson Hotel, Minneapolis, Minnesota**

**Be sure to mention that you will attend the meeting of the American College of Chest Physicians, and give arrival and departure dates.**

## LADIES' PROGRAM

### Saturday, November 29

12:30 p.m.—Luncheon and Style Show

Elizabethan Room, Kahler Hotel

6:00 p.m.—Cocktail Party

Regency Room and University Club

Lounge, Kahler Hotel

Courtesy of the Minnesota Chapter

American College of Chest Physicians

7:00 p.m.—Banquet

Elizabethan Room, Kahler Hotel

9:00 p.m.—Dancing

Royal Coach Room, Kahler Hotel

### Sunday, November 30

3:00-5:00 p.m.—Tea

At the home of

Mrs. Corrin H. Hodgson

Tours of the Mayo Clinic will be made on Saturday, Sunday and Monday mornings. The ladies are cordially invited to participate.

Rochester has beautiful stores for Christmas shopping. Information will be available at the ladies registration desk.

### Luncheon Reservations

Reservations for the luncheon on Saturday, November 29, may be made through the registration form on page 577. Tickets are \$2.75 each.

### Ladies Entertainment Committee

GRACE ROTH, Ph.D. .... *Chairman*  
MRS. MILTON W. ANDERSON ..... *Co-Chairman*

MRS. HOWARD A. ANDERSON

MRS. O. THERON CLAGETT

MRS. FRANCIS E. DONOGHUE

MRS. JAMES W. DUSHANE

MRS. JOSEPH E. GERACI

MRS. CORRIN H. HODGSON

MRS. GILES A. KOELSCH

MRS. R. DREW MILLER

MRS. HERMAN J. MOERSCH

MRS. ARTHUR M. OLSEN

MRS. JOHN R. PENIDO

MRS. GUSTAVUS A. PETERS

MRS. RAYMOND D. PRUITT

### 25th ANNUAL MEETING

SILVER ANNIVERSARY, AMERICAN COLLEGE OF CHEST PHYSICIANS  
AMBASSADOR HOTEL, ATLANTIC CITY, NEW JERSEY  
JUNE 3-7, 1959

### HOMEcoming MEETING

SILVER ANNIVERSARY, AMERICAN COLLEGE OF CHEST PHYSICIANS  
ALBUQUERQUE, NEW MEXICO  
OCTOBER 14-17, 1959



## ADVANCE REGISTRATION AND RESERVATION FORM

### American College of Chest Physicians

112 East Chestnut Street  
Chicago 11, Illinois

Enclosed please find my check in the amount of \$..... for reservations at the following functions to be held in Rochester/Minneapolis, November 29-30 and December 1, 1958.

### ROCHESTER, MINNESOTA

**Saturday, November 29**

#### LADIES' LUNCHEON \$2.75 each

Please reserve..... places at the luncheon

#### DINNER \$7.50 each

(Including cocktail party, dinner, and dance)

Please reserve..... places at the dinner

**Sunday, November 30**

#### ROUND TABLE LUNCHEONS \$2.75 each

- 1) Disorders of Esophageal Motility
- 2) Bronchography, Indications and Techniques
- 3) Surgical Treatment of Acquired Valvular Heart Disease
- 4) Early Detection of Emphysema

First Choice, No. .... Second Choice, No. ....

#### DUTCH TREAT BUFFET \$3.25 each

Please reserve..... places at the buffet.

### MINNEAPOLIS, MINNESOTA

**Monday, December 1—DINNER \$6.00 each**

Please reserve..... places at the dinner.

**IMPORTANT:** Please complete reverse side. Thank you.

### NOTES

Applications for reservations at the round table luncheons will be accepted in the order received. Your luncheon and dinner tickets will be available at the College registration desk, Hotel Kahler Mezzanine, Rochester, and at the Radisson Hotel in Minneapolis. Please make checks payable to the *AMERICAN COLLEGE OF CHEST PHYSICIANS*.

The ladies are cordially invited to attend the dinners in both Rochester and Minneapolis.



**INTERIM SESSION  
ADVANCE REGISTRATION FORM**

Name .....

Address .....

City and State .....

I AM..... AM NOT..... planning to attend the meeting in Minneapolis,  
December 1, 1958.

Please reserve..... places on the chartered bus leaving Rochester at  
1:00 p.m., Monday, December 1, for Minneapolis. Tickets \$3.15 each.

I have requested reservations at the Kahler Hotel, Rochester

.....Hotel, Rochester

Arrival date..... Departure date.....

I have requested reservations at the Radisson Hotel, Minneapolis

.....Hotel, Minneapolis

Arrival date..... Departure date.....

Accompanied by:.....

Remarks .....

.....

.....

**Please Return This Form Promptly.  
Thank you.**

## MEDICAL SERVICE BUREAU

### POSITIONS AVAILABLE

**Physician** wanted for moderate-sized chest disease hospital. Residency training pulmonary diseases. Man, 28-40 years of age, single. Graduate approved school, one year internship at least. Maintenance. State salary. Write: Medical Director, Will Rogers Memorial Hospital, Saranac Lake, New York.

**Physician** wanted interested in pulmonary diseases for 170-bed state supported tuberculosis hospital established 3 years. Active surgical program, out-patient service, x-ray and laboratory. Consultants in all branches. U. S. citizenship and Alabama medical license or eligibility therefor required. Salary \$8500 to \$9500 depending on qualifications. Quarters to be made available. Apply: Medical Director, Sixth District Tuberculosis Hospital, 800 St. Anthony Street, Mobile, Alabama.

**Physician** wanted for approved residency in pulmonary diseases. Accredited bicounty hospital, 219 beds pulmonary diseases, 30 beds rehabilitation chronic illness. Starting salary \$600 monthly, includes furnished modern house for family. Must be eligible for California licensure. Write: Medical Director, Tulare-Kings Counties Hospital, Springville, California.

#### **The Kahler Hotel Rochester, Minnesota**

I am planning to attend the Interim Session, American College of Chest Physicians, Rochester, Minnesota, November 29-30 and December 1, 1958. Please reserve the following accommodations:

Single Room \_\_\_\_\_ Double Room \_\_\_\_\_ Suite \_\_\_\_\_

Arrival Date \_\_\_\_\_ Hr. \_\_\_\_\_ Departure \_\_\_\_\_

Name \_\_\_\_\_

Accompanied by \_\_\_\_\_

Address \_\_\_\_\_

City \_\_\_\_\_ State \_\_\_\_\_

## CALENDAR OF EVENTS

### National Meeting

#### Interim Session

American College of Chest Physicians

Rochester, Minnesota, November 29-30, December 1, 1958

### Semi-Annual Meeting, Board of Regents

American College of Chest Physicians

Minneapolis, Minnesota, December 1, 1958

## POSTGRADUATE COURSE

4th Annual Course on Diseases of the Chest

San Francisco, California, February 16-20, 1959

## CHAPTER MEETING

Potomac Chapter, Washington, D. C., November 23, 1958



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200 Beds for Tuberculosis

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HENRY W. MALY, M.D. Director  
Cragmor Sanatorium  
Colorado Springs, Colorado



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